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(54) Title: WD-40-DERIVED PEPTIDES AND USES THEREOF

(57) Abstract

The present invention relates to a polypeptide composition effective to alter the activity of a first protein that interacts with a second protein, where the second protein contains at least one WD-40 region. The polypeptides of the present invention typically have between and 50 amino acids whose sequence is the same as a sequence of the same length in the WD-40 region of the second protein. The invention further includes a method of altering the activity of the above described first protein. In one embodiment of the invention the polypeptide composition is effective to alter the activity of a protein kinase C, where the protein kinase C interacts with a second protein, and the second protein contains at least one WD-40 region (e.g., RACK1).

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WD-40 - DERIVED PEPTIDES AND USES THEREOF

Field of the Invention

The present invention relates in general to compositions and methods of modulating the function of proteins involved in protein-protein interactions. It relates more specifically to modulating the function of a first protein of a pair of interacting proteins wherein a second protein of the pair contains a "WD-40" or "ß-transducin" amino acid repeat motif.

10 Background Art

Many intracellular processes are carried out or regulated by multi-subunit protein complexes that become active or repressed by the association or dissociation of individual polypeptide subunits.

One such group or family of proteins is related to the ß subunit of transducin. Members of this group are all at least somewhat homologous to the ß-subunit of transducin at the amino acid level, and contain a varying number of repeats of a particular motif identified in ß-transducin. The repeats have been termed "ß-transducin", or "WD-40" repeats (Fong, et al.).

Among the members of this protein family (Duronio, et al.) are the $G\beta$ subunits that couple many receptors to their intracellular effector molecules, $G\beta/\gamma$ subunits that anchor another protein kinase (the β -adrenergic receptor kinase, β ARK),

DNA binding proteins and yeast cell cycle proteins. All of these require a transient protein-protein interaction for their function. However, the sequences at the interface of these proteins and their partners have not been identified.

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Disclosure of the Invention

The invention includes, in one aspect, a polypeptide composition effective to alter the activity of a first protein, such as protein kinase C, or β -adrenergic receptor kinase (β ARK). The polypeptide blocks or inhibits an interaction, such as a binding interaction, between the first protein and a second protein containing a WD-40 region.

The polypeptide contains between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in the WD-40 region of the second protein.

The polypeptide may block the binding of the first to the second protein, or may be an agonist or antagonist of the first protein. The WD-40 region preferably has an amino acid sequence homologous or identical to the sequences defined by SEQ ID NO:76-261.

In a second embodiment, the invention includes a method of altering the activity of the first protein of the type defined above. The method includes selecting a polypeptide having between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in the WD-40 region of the second protein, and contacting the polypeptide with the first protein under conditions which allow the formation of a complex between the polypeptide and the first protein, where this interaction alters the activity of the first protein.

In one embodiment, the contacting is effective to inhibit the interaction between the first and second proteins. In another embodiment, the contacting is effective to stimulate the activity of the first protein.

In still another embodiment, the contacting is effective to inhibit the activity of the first protein.

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The polypeptide preferably has an amino acid sequence homologous or identical to the sequences defined by SEQ ID NO:76-261.

In a more specific aspect of the invention, the

invention includes a polypeptide composition effective to alter
the activity of protein kinase C, where the protein kinase C
interacts with a second protein, and the second protein contains
at least one WD-40 region. The polypeptide has between 4 and 50
amino acids whose sequence is the same as a sequence of the same
length in the WD-40 region of the second protein.

In a preferred embodiment, the second protein is a receptor for activated protein kinase C, and has the sequence represented by SEQ ID NO:27.

In other specific embodiments, the polypeptide is (i)

an agonist of protein kinase C, and the polypeptide has the
sequence represented by SEQ ID NO:7; (ii) an antagonist of the
activity of protein kinase C; and/or (iii) an inhibitor of the
interaction between protein kinase C and the second protein. In
the latter embodiment, the polypeptide has sequence
corresponding to SEQ ID NO:4 or SEQ ID NO:7.

The WD-40 region preferably has an amino acid sequence homologous or identical to SEQ ID NO:69-75.

In a related embodiment, the invention includes a method of altering the activity of a protein kinase C that interacts with a second protein, where said second protein contains at least one WD-40 region.

The method includes selecting a polypeptide having between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in the WD-40 region of the second protein, and contacting the polypeptide with the protein kinase C under conditions which allow the formation of a complex between the polypeptide and the protein kinase C, where said interaction alters the activity of said protein kinase C.

Other aspects of the invention include the polypeptide
compositions of the invention wherein said polypeptide is
coupled to a solid support, as well as a method to bind
selectively said first protein which method comprises contacting
a sample putatively containing said first protein with the

polypeptide composition bound to solid support and removing any unbound components of the sample from said composition.

In still another aspect, the invention relates to a method to assess the interaction of a first protein with a 5 polypeptide represented by an amino acid sequence contained in a second protein, wherein said second protein contains at least one WD-40 region, which method comprises contacting a sample containing said first protein with a polypeptide composition wherein the polypeptide has between 4 and 50 amino acids whose sequence is the same as the sequence of the same length in the 10 WD-40 region of the second protein, and observing any interaction of the first protein with said polypeptide composition. The invention also concerns a method to assess the ability of a candidate compound to bind a first protein which method comprises contacting said first protein with a polypeptide composition which binds said first protein, wherein the polypeptide of said composition has between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in a WD-40 region of a second protein which interacts 20 with said first protein, in the presence and absence of said candidate compound; and measuring the binding of said polypeptide in the presence and in the absence of said candidate, wherein decreased binding of the polypeptide in the presence as opposed to the absence of said candidate indicates 25 that said candidate binds to said first protein.

In still another aspect, the invention is directed to recombinant materials for the production of the polypeptides of the invention and methods for their production.

These and other objects and features of the invention will become more fully apparent when the following detailed description of the invention is read in conjunction with the accompanying drawings.

Brief Description of the Figures

Figure 1A shows the cDNA sequence of rat brain RACK1.

Figure 1B shows an amino acid self-homology matrix analysis of RACK1.

Figure 1C shows the amino acid sequence of RACK1, aligned to show the seven WD-40 repeats represented in the molecule.

Figure 2 shows the results of an overlay assay to detect PKC binding to immobilized RACK1 in the presence and absence of PKC activators.

Figure 3 shows the results of an overlay assay to detect PKC binding to immobilized RACK1 in the presence and absence of WD-40-derived peptides.

Figure 4 shows the results of an overlay assay to detect binding of β PKC to either peptide I (SEQ ID NO:1) or peptide rVI (SEQ ID NO:7) immobilized on nitrocellulose membranes under various conditions.

Figure 5A shows the effects of injecting peptides I (SEQ ID NO:1) and rVI (SEQ ID NO:7) on PKC-mediated germinal vesicle breakdown (GVBD), a measure of insulin-induced oocyte maturation.

Figure 5B shows the effects of injecting peptides I (SEQ ID NO:1) and rVI (SEQ ID NO:7) on PKC-mediated germinal vesicle breakdown (GVBD) in the absence of insulin induction.

Figure 5C shows the effects of injecting peptide rIII (SEQ ID NO:4) on PKC-mediated germinal vesicle breakdown (GVBD) in the absence of insulin induction.

Figure 6 shows the distribution of βPKC in Xenopus oocytes between the cytosolic and membrane-associated fractions following microinjection of either injection solution, peptide I (SEQ ID NO:1) or peptide rVI (SEQ ID NO:7) with or without insulin stimulation.

Figure 7 shows the effects of peptides I and rVI on the sensitivity of β PKC to Arg-C endopeptidase.

Figure 8 shows the effects of peptides I and rVI on PKC autophosphorylation in the absence of PKC activators.

Figure 9 shows the effects of peptides I and rVI on PKC phosphorylation of histones in the absence of PKC

35 activators.

Figure 10 shows the effects of peptide rIII on PKC phosphorylation of histones in the absence of PKC activators.

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Figure 11 shows the amino acid sequence of the 56 kDa human protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 12 shows the amino acid sequence of the AAC-5 rich protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 13 shows the amino acid sequence of the B-TRCP protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 14 shows the amino acid sequence of the Betaprime-COP protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 15 shows the amino acid sequence of the CDC4 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 16 shows the amino acid sequence of the Chlam-3 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 17 shows the amino acid sequence of the COP-1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 18 shows the amino acid sequence of the CORO protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

25 Figure 19 shows the amino acid sequence of the Coronin p55 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 20 shows the amino acid sequence of the Cstf 50 kDa protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 21 shows the amino acid sequence of the bovine G-beta-1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 22 shows the amino acid sequence of the bovine 35 G-beta-2 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 23 shows the amino acid sequence of the drosophila G-beta protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 24 shows the amino acid sequence of the human 5 G-beta-1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 25 shows the amino acid sequence of the human G-beta-2 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 26 shows the amino acid sequence of the mouse G-beta protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

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Figure 27 shows the amino acid sequence of the drosophila groucho protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 28 shows the amino acid sequence of the squid GTP-binding protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 29 shows the amino acid sequence of the HSIEF 930 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 30 shows the amino acid sequence of the human 12.3 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 31 shows the amino acid sequence of the human IEF-7442 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 32 shows the amino acid sequence of the insulin-like growth factor binding protein complex with the WD-30 40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 33 shows the amino acid sequence of the rat insulin-like growth factor binding protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 34 shows the amino acid sequence of the human LIS1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

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Figure 35 shows the amino acid sequence of the MD6 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 36 shows the amino acid sequence of the yeast 5 MSI1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 37 shows the amino acid sequence of the mouse pc326 MUS protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 38 shows the amino acid sequence of the ORD RB1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 39 shows the amino acid sequence of the periodic trp protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 40 shows the amino acid sequence of the PLAP protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 41 shows the amino acid sequence of the retinoblastoma binding protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 42 shows the amino acid sequence of the S253 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 43 shows the amino acid sequence of the SOF1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 44 shows the amino acid sequence of the STE4 yeast protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 45 shows the amino acid sequence of the TF1 transcription factor protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 46 shows the amino acid sequence of the TUP1 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 47 shows the amino acid sequence of the TUP1 homolog protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 48 shows the amino acid sequence of the YCU7 5 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 49 shows the amino acid sequence of the YCW2 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 50 shows the amino acid sequence of the YKL25 10 protein with the WD-40 repeats aligned and putative binding peptide regions delineated by a box.

Figure 51 shows the amino acid sequence of the YRB140 protein with the WD-40 repeats aligned and putative binding 15 peptide regions delineated by a box.

Detailed Description of the Invention

I. <u>Definitions</u>

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Unless otherwise indicated, all terms used herein have the same meaning as they would to one skilled in the art of the 20 present invention. Practitioners are particularly directed to Current Protocols in Molecular Biology (Ausubel) for definitions and terms of the art.

Abbreviations for amino acid residues are the standard 3-letter and/or 1-letter codes used in the art to refer to one 25 of the 20 common L-amino acids. Likewise, abbreviations for nucleic acids are the standard codes used in the art.

An "amino acid group" refers to a group of amino acids where the group is based on common properties, such as hydrophobicity, charge, or size.

A "conserved set" of amino acids refers to a contiguous sequence of amino acids that is conserved between members of a group of proteins. A conserved set may be anywhere from two to over 50 amino acid residues in length. Typically, a conserved set is between two and ten contiguous residues in The individual positions within a conserved set each typically comprise one of several amino acids, selected from an amino acid group(s). In cases where a residue is 100% conserved at a particular position, the conserved set sequence will contain only that residue at that position. For example, for the two peptides WRTAA (SEQ ID NO:263) and WRTAV (SEQ ID NO:264), there are 4 identical positions (WRTA; SEQ ID NO:265) and one position where the residue is an "A" or a "V".

Proteins are typically long chains of amino acid based polyamides (polypeptides) capable of creating secondary and tertiary structure. Proteins may be composed of one, two or more polypeptide chains and may further contain some other type of substance in association with the polypeptide chain(s), such as metal ions or carbohydrates. The size of proteins covers a rather wide range from ~5,000 to several hundred thousand g/mole. The 5,000 figure corresponds to the presence or roughly 40-45 amino acids.

Unless otherwise indicated, the sequence for proteins and peptides is given in the order from the amino terminus to the carboxyl terminus. Similarly, the sequence for nucleic acids is given in the order from the 5' end to the 3' end.

The term "interacting proteins" refers to a pair of polypeptides that can form a stably-associated complex due to, for example, electrostatic, hydrophobic, ionic and/or hydrogenbond interactions under physiological conditions.

Proteins smaller than about 5,000 g/mole are typically referred to as polypeptides or simply peptides (Bohinski).

Two amino acid sequences or two nucleotide sequences are considered homologous (as this term is preferably used in this specification) if they have an alignment score of >5 (in standard deviation units) using the program ALIGN with the mutation gap matrix and a gap penalty of 6 or greater (Dayhoff).

The two sequences (or parts thereof) are more preferably homologous if their amino acids are greater than or equal to 50%, more preferably 70%, still more preferably 80%, identical when optimally aligned using the ALIGN program mentioned above.

A peptide or peptide fragment is "derived from" a

parent peptide or polypeptide if it has an amino acid sequence
that is identical or homologous to the amino acid sequence of
the parent peptide or polypeptide. Homologous peptides are
defined above. Exemplary derived peptides are peptide rIII (SEQ)

ID NO:4) and peptide rVI (SEQ ID NO:7), which are derived from the third and seventh WD-40 repeats of RACK1 (SEQ ID NO:27), respectively.

The term "expression vector" refers to vectors that

5 have the ability to incorporate and express heterologous DNA
fragments in a foreign cell. Many prokaryotic and eukaryotic
expression vectors are commercially available. Selection of
appropriate expression vectors is within the knowledge of those
having skill in the art.

The term "PKC" refers to protein kinase C, or C-kinase.

The term "RACK" refers to receptor for activated C-kinase.

The term "PS" refers to phosphatidylserine.

The term "DG" refers to diacylglycerol.

The term "PL" refers to phospholipids. Phospholipids include both phosphatidylserine and diacylglycerol.

The term "GVBD" refers to germinal vesicle breakdown, a measure of insulin-induced maturation in Xenopus oocytes.

The term "PCR" refers to polymerase chain reaction.

The term "NMR" refers to nuclear magnetic resonance.

The term "etaARK" refers to eta-adrenergic receptor

kinase.

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II. General Overview of Invention.

The invention relates to interacting proteins, at least one of which contains an amino acid sequence with one or more of the characteristic repeats termed WD-40 (Fong, et al.).

According to one aspect of the invention, the function of a first protein of a pair of interacting proteins may be modulated, altered or disrupted by the addition, to a solution or medium containing the protein, of a peptide having a sequence that is identical or homologous to a part of the sequence of a WD-40 motif-containing repeat present in a second protein of the pair of interacting proteins.

The modulation or disruption of function of the first protein is due to the binding or association of the WD-40-derived peptide, termed "binding peptide", with the first

protein. The consequences of the binding or association of the binding peptide with the first protein depend on the sequence of the peptide.

Typically, the presence of the binding peptide will inhibit the binding of the first protein to the second protein. This binding may be assayed in vitro by, for example, an overlay assay, whereby the degree of binding of one protein to another may be assessed. Several adaptations of overlay assays applied to embodiments of the present invention are described herein.

Regardless of whether or not the WD-40-derived peptide affects the association of the first protein with the second protein, the peptide may alter or modulate defined activities of the first protein. These activities may be assayed by a variety of methods in vivo and/or in vitro. The method(s) employed depend on the protein whose activity is being measured.

An exemplary first protein of a pair of interacting proteins is protein kinase C (PKC). Upon activation, PKC interacts with receptors for activated C kinase (RACKs), at least one of which (RACK1) contains WD-40 repeats. Several assays for determining the activity of PKC in the presence and in the absence of peptides derived from the WD-40 region of RACK1 are detailed herein.

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Certain "interacting proteins" interact only after one or more of them has been stimulated by an exogenous or endogenous factor(s). For instance, PKC, as shown herein, does not bind to RACK proteins until it has been activated by, for example, phosphatydilserine (PS), diacylglycerol (DG) and calcium. However, peptides derived from WD-40 repeats of a second protein of such a pair may be able to associate with or bind to the first protein even in the absence of activators of the first protein, and in so doing, affect the function of the first protein (e.g. activate, inactivate, potentiate, sensitize, desensitize, alter the specificity, etc.).

Binding peptides derived from WD-40 repeats of a

second protein of a pair of interacting proteins, may be useful
as specific agonists, antagonists, potentiators of function, and
the like, of the first protein of the pair. These properties
may make the peptides useful in a number of applications, for

example, direct use in therapeutic applications or as lead compounds for the development of other therapeutic agents, e.g., small organic molecules.

III. Advantages of the Invention for the Inhibition of Activated 5 PKC Binding to RACK1.

Protein kinase C (PKC) is a family of at least 10 isozymes that share common structures and biochemical characteristics. It has been demonstrated that several isozymes are present within a single cell type, and it has been assumed that individual PKC isozymes are involved in different cellular functions. However, so far, the available activators and inhibitors of PKC do not appear to be isozyme-specific. Therefore, it is currently impossible to determine the role of individual PKC isozymes in normal cellular functions as well as in disease.

PKC activation by, for example, diacylglycerol and calcium, induces the translocation of PKC from a soluble (cytosolic) to a cell particulate (membrane-associated) fraction, as shown in experiments herein (Example 8). Activated PKC is stabilized in the cell particulate fraction by binding to membrane-associated receptors (receptors for activated C-Kinase, or RACKs).

In experiments done in support of the present invention and described herein, a clone (pRACK1) encoding a RACK has been isolated (Example 1). RACK1 belongs to a growing family of proteins that are homologous to the ß-subunit of transducin and contain the WD-40 motif (Fong, et al.). It was demonstrated that peptide I (SEQ ID NO:1) binds to purified PKC (see Example 6 and Fig. 4), inhibits the binding of PKC to purified recombinant RACK1 protein (see Example 4 and Fig. 3), and inhibits PKC activity in several in vivo and in vitro assays (see Examples 7-11 and Figs. 5-9).

Peptide I (SEQ ID NO:1) is homologous to a sequence identified in the sixth WD-40 repeats of RACK1 (see Fig. 1C). A synthetic peptide was prepared based on this sequence (peptide rVI; SEQ ID NO:7; underlined amino acids in repeat VI of Fig. 1C). Six more peptides were also prepared based on the

corresponding regions in repeats I-V and VII (peptides rI-rV, rVII; SEQ ID NO:2-6, 8; underlined regions in corresponding repeats, Fig. 1C). Some of the peptides were also found to inhibit the binding of PKC to RACK1 (see Example 4 and Fig. 3).

In addition, some of the peptides were found to bind to purified PKC (see Example 6, Fig. 4), partially activate PKC in the absence of other activators (peptide rVI; see Examples 7, 10, 11 and Figs. 5, 8 and 9), and potentiate the effects of known PKC activators on the enzyme (see Examples 7-9 and Figs. 5-7).

In Xenopus oocyte maturation studies (see, for instance, Example 7), peptide rVI (SEQ ID NO:7) is an agonist of β PKC. Peptide rIII, while less potent, is also an agonist of PKC; it enhances insulin-induced oocyte maturation at 50 and 500 μ M.

In cardiac myocytes, norepinephrine (NE, 2μ M) causes translocation of δ and ϵ PKC isozymes from the cytosolic to the particulate fraction. Introduction into cardiac myocytes of peptide rIII, and to a lesser extent peptide rVI, caused an immediate translocation of δ and ϵ PKC isozymes in the absence of hormone stimulation. This peptide-induced translocation was followed by degradation of δ and ϵ PKC isozymes. Moreover, NE-induced translocation is further enhanced in cells containing peptide rIII.

In contrast, introduction of peptide I to these cells does

25 not affect PKC distribution in the absence of hormone
stimulation, nor does it induce PKC degradation. Furthermore,
NE-induced translocation is inhibited by peptide I. Similar
concentrations of a number of control peptides did not affect
PKC distribution or degradation in control or NE-treated cells.

In studies on rat cardiac myocytes, peptide rIII induced δ PKC and ϵ PKC activation that was followed by degradation of these activated isozymes.

Peptide rVI also augments hormone-induced translocation of PKC isozymes (see, for example, Example 8 and Fig. 6). In contrast, peptide I (SEQ ID NO:1) inhibited hormone-induced translocation of PKC isozymes (Example 8, Fig 6) and did not cause degradation.

The data summarized above demonstrate that peptides derived from WD-40 repeats of RACK1 can serve as PKC agonists and antagonists in vivo, and suggest that peptides derived from WD-40 regions of RACK1 contain at least part of the protein-protein interface between PKC and RACK1.

Furthermore, the results suggest that (i) WD-40 repeats present in other proteins, such as $G\beta$ subunit, may also be located at or near a surface involved in protein-protein interactions, (ii) peptides derived from these repeats may be effective in disrupting the interactions of the proteins with their partners (e.g. β -adrenergic receptor kinase (β ARK), (iii) the peptides may modulate or alter the activity of the proteins with which the WD-40 repeat-containing proteins interact, and (iv) the peptides may therefore have specific biological effects when administered in vivo.

IV. Identification of Pairs of Interacting Proteins.

A. <u>Biochemical Approaches.</u>

Novel interacting proteins may be identified and isolated by a number of methods known to those skilled in the art. For example, monoclonal antibodies raised to a mixture of antigens, such as a particular tissue homogenate, may be characterized and used to immunoprecipitate a single class of antigen molecules present in that tissue. The precipitated proteins may then be characterized further, and used to coprecipitate other proteins with which they normally interact (Hari, et al., Escobedo, et al.).

An alternate method to identify unknown polypeptides that interact with a known, isolated protein is by the use of, for example, an overlay assay (Wolf, et al., Mochly-Rosen, et al., 1991). A mixture (such as a fraction of a tissue homogenate, for example, a Triton-insoluble protein fraction) potentially containing proteins that bind to a known, isolated protein can be resolved using PAGE, blotted onto a nitrocellulose or nylon membrane, and contacted with a solution containing the known protein and any necessary co-factors or small molecules. After washing, the membrane can be contacted

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with a probe for the known protein, for example an antibody or a mixture of antibodies, and the signal visualized.

B. <u>Molecular Approaches</u>.

Putative binding proteins of a known protein may be isolated from tissue homogenates, as described above. Alternatively, DNA clones encoding putative binding proteins may be identified by screening, for example, an appropriate cDNA expression library. Expression libraries made from a wide variety of tissues are commercially available (for example, from Clonetech, Palo Alto, CA). Expression libraries may also be made de novo from organisms and tissues of choice by practitioners skilled in the art.

The screening of expression libraries for clones expressing a protein or protein fragment of interest may be readily accomplished using techniques known in the art, for example, an overlay assay.

An overlay-assay screening method may be used to identify clones expressing a (known or unknown) protein or protein fragment that binds to a probe in hand. The probe may be a protein postulated to be involved in protein-protein interactions with a protein expected to be present in a cDNA library selected for screening (as was the case for the cloning of RACK1, detailed in Example 1).

Actual screening of a selected cDNA library may be accomplished by inducing plated clones to express cloned 25 exogenous sequences, transferring replicas of the induced plaques or colonies to filter membranes, and screening the membranes with an appropriate probe. According to this method, lifts of filters (for example, nylon or nitrocellulose) from an appropriately-induced cDNA library plates (induced by, for 30 example, IPTG) are washed, blocked, and incubated with a selected probe for a period of time sufficient to allow the selected probe(s) to bind specifically to polypeptide fragments present on the filters. The filters may then be washed and reacted with a reagent (for example, antibodies such as alkaline 35 phosphatase-conjugated goat anti-rabbit or anti-mouse antibodies, available from Boehringer Mannheim Biochemicals,

Indianapolis, IN). Additional reactions may be carried out as required to detect the presence of bound probe.

One such overlay assay, described in Example 1, was used to screen a rat brain cDNA expression library for proteins 5 that bind purified PKC in the presence of PKC activators (phosphatydilserine, diacylglycerol and calcium). The filters were screened with a mixture of rat brain PKC isozymes (lpha, eta, γ , δ , ϵ and ζ). Following a series of washes, bound PKC isozymes were detected with a mixture of anti-lpha, eta, γ PKC mouse monoclonal antibodies, and anti- δ , ϵ and ζ PKC rabbit polyclonal 10 antibodies. Bound antibodies were detected using alkaline phosphatase-conjugated goat anti-rabbit or anti-mouse antibodies and 5-bromo-4-chloro-3-indoyl phosphate p-toluidine salt as a substrate.

Once a clone is identified in a screen such as the one 15 described above, it can be isolated or plaque purified and sequenced. The insert may then be used in other cloning reactions, for example, cloning into an expression vector that enables efficient production of recombinant fusion protein.

20 Examples of appropriate expression vectors are pGEX (Smith, et al., 1988) and pMAL-c2 (New England BioLabs, Beverly, MA). expression vector containing an insert of interest may be used to transform appropriate host cells, such as E. coli, and the transformed host cells can be used to produce the recombinant protein in large amounts.

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Typically, a recombinant protein is expressed in tandem with a bacterial or viral gene product (endogenous polypeptide) as part of a fusion protein. The junction between the endogenous polypeptide and the recombinant protein typically 30 includes a recognition site for a rare-cutting protease. The endogenous peptide may be designed to incorporate a unique affinity tag (a short peptide sequence) to facilitate the purification of the fusion protein with an affinity reagent, such an antibody directed against the affinity tag. recombinant protein may then be purified from the fusion protein using the appropriate protease.

Purified recombinant protein may be used in a number of ways, including in an overlay binding assay to screen for

peptides or substances that inhibit binding between the recombinant protein and an interacting protein.

An example of the use of a cDNA clone to express protein is detailed in Example 2. RACK1 cDNA, isolated as described above and in Example 1, was subcloned into an expression vector (pMAL-c2, New England BioLabs, Beverly, MA) capable of expressing a cloned insert in tandem with maltose-binding protein (MBP). The vector containing the RACK1 insert was used to transform TB1 E. coli, which were then induced with IPTG. The cells produced a 78 kDa fusion protein comprised of RACK1 fused to the MBP. The overexpressed fusion protein was purified on an amylose affinity column according to the manufacture's protocol (New England BioLabs, Beverly, MA) and incubated with protease Xa to separate the expressed insert from obtained.

V. Identification of WD-40 Repeats.

According to a method of the present invention, protein-protein interactions can be disrupted and/or the activity of an interacting protein can be altered, given at least one of the interacting proteins contains a WD-40 motif, or region, with a peptide(s) derived from a WD-40 repeat(s) of one of the proteins.

WD-40 repeats are typically found in a family of proteins having at least a limited homology with the ß subunit 25 of transducin. WD-40 repeats present in a selected member of this family can be identified by (A) performing a self-homology analysis on a selected protein using a homology matrix (performed by, for example, the computer program DNA Strider 1.2, available from Christian Marck, Service de Biochemie et de 30 Genetique Moleculaire, Department de Biologie Cellulaire et Moleculaire, Direction des Sciences de la Vie - CEA - FRANCE), (B) aligning sequences comprising the repeating elements revealed by the homology matrix analysis, and (C) identifying conserved amino acid residues that typically serve to define a 35 WD-40 repeat. The steps are discussed individually, below.

Homology matrix analysis.

Determining whether a particular amino acid sequence Α. contains repeated motifs may be accomplished by a number of methods known to those skilled in the art. They range from a 5 simple visual inspection of the sequence to the use of computer programs which can identify repeated motifs. One widelyimplemented computer-assisted method is to generate a selfhomology matrix. A self-homology matrix computes the homology of each amino acid residue in a particular sequence with every 10 other residue in that sequence. The homology scores are stored in a 2-dimensional matrix.

Values higher than a selected criterion level are flagged and displayed as points on an x-y coordinate. The xand y-axes correspond to consecutive amino acid positions in the 15 sequence.

An example of a self-homology matrix analysis is shown in Figure 1B. The matrix was generated using the computer program DNA Strider 1.2 (Christian Marck, Service de Biochemie et de Genetique Moleculaire, Department de Biologie Cellulaire 20 et Moleculaire, Direction des Sciences de la Vie - CEA - FRANCE) with the amino acid sequence of RACK1 (SEQ ID NO:27) with a window setting of 21 and a stringency of 6. Some typical features of a self-homology matrix are evident in the figure. The graph shows a "primary" diagonal line extending from the 25 origin with a slope of unity, corresponding to the fact that the sequence is identical to itself. If the sequence contains repeating elements, as RACK1 does, there will be other, shorter sets of contiguous points arranged in diagonal lines substantially parallel to the primary diagonal and offset from 30 the primary diagonal in the x- or y-directions. These shorter lines identify the locations of repeating elements with the sequence. Each repeating element will result in two sets of displayed points, symmetrically distributed about the primary diagonal.

The data displayed in a homology matrix analysis can be used to locate and roughly align the sequences of repeating elements for a more detailed analysis. The horizontal band delineating the region between ~100 and ~130 on the y-axis in

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Fig. 1B highlights the fact that portions of that region of RACK1, that is, the amino acids between about amino acid 100 and amino acid 130, are repeated a total of seven times in the sequence of RACK1. Arrows point to the repeats in the homology matrix. For purposes of rough alignment, the short diagonal lines pointed out by the arrows can be extended to the horizontal line at amino acid ~100 on the y-axis, and the x-axis location corresponding to the intersection be noted. For example, the intersection corresponding to the second repeat (second arrow from the left) is at x=~50).

Values determined in this manner may then be used to align the amino acid sequence of the repeats with each consecutive repeat beneath the preceding one, the start of each repeat corresponding approximately to the amino acid position determined by the analysis in the preceding paragraph. The amino acid sequence of RACK1, aligned in this manner, is shown in Fig. 1C.

Most commercially-available DNA and protein sequence analysis programs have the capability to perform a self-homology matrix analysis. One example is the program DNA Strider 1.2 (Christian Marck, Service de Biochemie et de Genetique Moleculaire, Department de Biologie Cellulaire et Moleculaire, Direction des Sciences de la Vie - CEA - FRANCE).

Once the repeating elements are identified and the sequences corresponding to repeating elements are roughly aligned, one may proceed to define the degree of homology among the individual repeats at the specific positions within the repeats, as is described below.

B. Aligning amino acid sequences.

If a self-homology matrix was used to obtain a crude alignment, the sequences may aligned by eye on a personal computer or the like using, for example, a text editor, a drawing program or a sequence-analysis program. Examples of programs effective to accomplish an alignment include "MACDRAW PRO" (Claris Corp., Santa Clara, CA) and "WORD" (Microsoft Corp., Redmond, WA), both of which are available for "MACINTOSH" series computers (Apple Computer Corporation, Cupertino, CA), as

well as IBM-compatible computers running "WINDOWS" (Microsoft Corp.).

Amino acid sequences corresponding to internal repeats can also be aligned automatically using a protein sequence analysis program, such as "MACVECTOR" (Eastman Kodak Co., New Haven, CT).

According to a method of the invention, aligned sequences are examined further to determine if they fulfil criteria to be defined as WD-40 repeats. These criteria are detailed in part C, below.

C. Amino acid residues that define a WD-40 repeat.

Upon completion of steps outlined in parts A and B above, that is, determining whether a particular protein contains internal repeats, and if so, aligning those repeats, it is necessary to determine whether the aligned repeats contain WD-40 regions.

A WD-40 motif is roughly defined as a contiguous sequence of about 25 to 50 amino acids with relatively-well conserved sets of amino acids at the two ends (amino- and carboxyl-terminal) of the sequence. Conserved sets of at least one WD-40 repeat of a WD-40 repeat-containing protein typically contain conserved amino acids at certain positions. The amino-terminal set, comprised of two contiguous amino acids, often contains a Gly followed by a His. The carboxyl-terminal set, comprised of six to eight contiguous amino acids, typically contains an Asp at its first position, and a Trp followed by an Asp at its last two positions.

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A more accurate definition of a WD-40 motif incorporates the observation that while specific residues, such as those identified above, are not always conserved within a WD-40 motif, conserved positions within the motif are typically occupied by residues selected from a restricted class of amino acids.

In order to better define the class of conserved residues at selected positions, it is necessary to group amino acids on the basis of certain common properties. A functional way to define common properties between individual amino acids

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is to analyze the normalized frequencies of amino acid changes between corresponding proteins of homologous organisms (Schulz). According to such analyses, groups of amino acids may be defined where amino acids within a group exchange preferentially with each other, and therefore resemble each other most in their impact on the overall protein structure (Schulz). Examples of amino acid groups defined in this manner, some of which are used in the definition of a WD-40 motif herein, include:

- (i) a charged group, consisting of Glu and Asp, Lys, Argand His,
 - (ii) a positively-charged group, consisting of Lys, Arg and His,
 - (iii) a negatively-charged group, consisting of Glu and Asp,
- (iv) an aromatic group, consisting of Phe, Tyr and Trp,(v) a nitrogen ring group, consisting of His and Trp,
 - (vi) a large aliphatic nonpolar group, consisting of Val,
 - (vii) a slightly-polar group, consisting of Met and Cys,
 (viii) a small-residue group, consisting of Ser, Thr, Asp,
 Asn, Gly, Ala, Glu, Gln and Pro.
 - (ix) an aliphatic group consisting of Val, Leu, Ile, Met and Cys, and
 - (x) a small hydroxyl group consisting of Ser and Thr.
- In addition to the groups presented above, each amino acid residue may form its own group, and the group formed by an individual amino acid may be referred to simply by the one and/or three letter abbreviation for that amino acid commonly used in the art.
- A "WD-40" motif is defined herein as a contiguous set of amino acids between (inclusive) two sets of relatively well conserved residues, termed herein as an "amino-terminal set" and a "carboxyl-terminal set".
- The amino-terminal set contains two adjacent amino acids. The residue at the first position is typically selected from groups ii, vi or viii, while the residue at the second position is typically selected from groups i, x or Ile. The first and second positions will often consist of Gly and His,

respectively. The Gly and His residues are typically present in at least one of the aligned repeats of a WD-40-containing protein.

The carboxyl-terminal conserved set typically includes 5 eight residues, but may contain as few as six residues. The most well-conserved residue in WD-40 motifs identified thus far is an Asp residue, comprising the first amino acid of the carboxyl-terminal conserved set. It is present in virtually all WD-40 repeats illustrated herein. In those repeats where it is 10 not present, the position is occupied by a residue from groups iii or Gly.

The last two amino acids in the carboxyl-terminal conserved set are typically selected from groups iv or Ile, and groups i or viii, respectively. The most commonly used residue at the first of these positions is Trp. It is typically present in at least one of the WD-40 repeats of any given protein. 15 second position is occupied less consistently by a single residue, but is often occupied by Asp. The Trp-Asp (WD) combination is part of the namesake of WD-40 repeats.

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The amino acids present in the internal portion of the carboxyl-terminal conserved set are less well-conserved than the terminal residues, and their total number may differ by up to two residues in different WD-40 repeats. The third position in from the carboxyl-terminal end of the carboxyl-terminal 25 conserved set is typically selected from groups viii or ix, more typically ix. The fifth position in from the carboxyl-terminal end of the carboxyl-terminal conserved set is also typically selected from groups viii or ix, more typically ix.

The length of a WD-40 repeat, including the amino-30 terminal and carboxyl-terminal conserved sets is typically between about 25 and about 50 residues, more typically between about 29 and 34 residues. The distribution arises primarily from differences in the number of residues present between the amino-terminal and carboxyl-terminal conserved sets.

The number of WD-40 repeats in a particular protein can range from two to more than eight. The average number is 35 about 5.

A determination of whether or not a set of aligned internal repeats are WD-40 repeats can be facilitated by an examination of all of the repeats as a whole, rather than an examination of each repeat individually. This is in part because not all of the aligned repeats will necessarily contain all of the conserved sequences that serve to identify WD-40 repeats, although the conserved residues will typically appear in at least one of the repeats.

For example, Fig. 1C shows the RACK1 amino acid sequence aligned to illustrate the internal repeats present in the sequence. All of the repeats are WD-40 repeats, even though the amino-terminal conserved set of repeat VI, for instance, contains an "LD" as opposed to the more usual "GH", and the carboxyl-terminal conserved set contains a "G" at its first position, as opposed to the highly-conserved "D". Similarly, the carboxyl-conserved set of, for example, repeat I, contains a "WK" at the last to positions, as opposed to the more usual "WD".

of residues will be well-conserved in the WD-40 repeats of a selected protein, even though they may not be conserved in WD-40 repeats in general. Such residues or sets of residues may be useful in several ways. For example, they may be used in performing an alignment of internal repeats in a selected protein, as described in part B, above. The residues may also be useful for identifying regions based on which effective binding peptides may be designed (see section VI., below).

D. <u>Identification of WD-40 repeats in RACK1</u>.

In experiments done in support of the present
invention, a protein that binds to activated PKC was cloned and
sequenced (see Example 1). Sequence analysis of the deduced
amino acid sequence revealed the presence of repeats, which were
aligned and are shown in Figure 1C.

The aligned repeats were identified as WD-40 repeats

35 by application of the criteria identified in parts A, B and C

above. For example, the conserved amino-terminal set in repeats

I, II, III and V consists of the typical "GH", whereas in

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repeats IV, VI and VII, the set consists of other residues.

These other residues, however, are contained in at least one of the amino acid groups identified above as conserved at the appropriate position. The conserved carboxyl-terminal set contains the highly-conserved "D" at its first position in all repeats except repeat VI. The second-to-last position of this set contains the relatively-well conserved "W" in each repeat, while the last position contains the typical "D" in repeats II, V and VI, and other residues in the other repeats.

Taken together, these data indicate that the repeats contained in RACK1 are WD-40 repeats. The data also illustrate that not all repeats contain all of the elements typical of a WD-40 motif, but that when the repeats are aligned and viewed together as a whole, a WD-40 motif is apparent in all repeats.

Data were compiled in support of the present invention to illustrate how WD-40 repeats in various proteins may be identified, and to illustrate the diversity of amino acid sequences that may be properly identified as WD-40 repeats by those skilled in the art following the guidance set forth herein. Two methods that were used to identify WD-40-containing protein sequences are detailed in Example 7.

In the first method, proteins identified in their description as having a homology to β -transducin were examined as detailed in parts B-D, above, for WD-40 repeats. 30 proteins were identified in this manner. The amino acid sequences of these proteins, with the WD-40 regions aligned and delineated, are shown in Figs. 12-18, 20-27, 29-30, 34-35, 37-38, 40 and 42-50. The sequences are represented in the Sequence Listing as SEQ ID NO:29-35, 37-44, 46-47, 51-52, 54-55, 57 and 59-67.

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In the second method, proteins whose sequences were homologous to a consensus WD-40 motif (SEQ ID NO:262), were identified and examined for WD-40 repeats. Ten additional proteins containing WD-40 repeats were identified with this strategy. The amino acid sequences of those proteins, with the WD-40 repeats aligned and delineated, are shown in Figs. 11, 19, 28, 31-33, 36, 39, 41 and 51. The sequences are represented in

the Sequence Listing as SEQ ID NO:28, 36, 45, 48-50, 53, 56, 58, and 68.

Other types of searches may be equally effective at identifying proteins which may contain WD-40 repeats. For example, on-line databases such as GenBank or SwissProt can be searched, either with an entire sequence of a WD-40-containing protein, or with a consensus WD-40 repeat sequence. Various search algorithms and/or programs may be used, including FASTA, BLAST or ENTREZ. FASTA and BLAST are available as a part of the GCG sequence analysis package (University of Wisconsin, Madison, Wisconsin). ENTREZ is available through the National Center for Biotechnology Information, National Library of Medicine, National Institutes of Health, Bethesda, MD.

Sequences identified with a protein homology search are then analyzed as described in parts A, B and C, above, to identify potential WD-40 motifs. Once located, the motifs can be aligned, and effective binding peptides may be designed.

F. Identification of WD-40 regions in novel polypeptides.

WD-40 repeats may be identified in a novel polypeptide

by, for example, the methods described in parts A-D above. It

will be appreciated, however, that step A above (homology

matrix) is not required in the identification of WD-40 repeats.

Following the guidance of the present invention, one skilled in

the art may, for instance, identify a WD-40 motif while scanning

the sequence of some, perhaps novel, polypeptide merely through

a recognition of one or more of the features characteristic of

WD-40 repeats.

The precise methods by which one skilled in the art arrives at the conclusion that a particular motif is a WD-40 repeat is less relevant to the present invention than is the use of sequences derived from WD-40 motifs, regardless of how they are identified, to design peptides effective to alter or modulate the activity of one member of a pair of interacting proteins and/or to disrupt protein-protein interactions.

35 VI. Identification of Activity-altering Peptides.

Upon the alignment and recognition of WD-40 repeats in a particular protein, one may proceed to design a peptide or a set of peptides that may be effective to associate with or bind to the protein with which the WD-40-containing protein normally 5 associates. Such a binding or association may be expected to alter or modulate the activity of the protein and/or disrupt the association of the pair of interacting proteins.

The sequence of such a peptide will typically be homologous, if not identical to, a contiguous amino acid 10 sequence contained within at least one of the WD-40 repeats. Examples of the selection of WD-40-derived peptides effective to disrupt protein-protein interactions are detailed in parts C and D below, for RACK-PKC and $G\beta/\gamma$ - β ARK interactions, respectively.

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Choosing an appropriate region within a WD-40 repeat. Α.

Putative binding peptides may be selected from any portion of a WD-40 repeat. If it is desired to obtain a degree of discrimination between the various WD-40-containing proteins, peptides should be chosen from the region between, and not including, the amino-terminal and carboxyl-terminal conserved sets. This "central region" typically shows greater sequence diversity between different WD-40-containing proteins than the 20 terminal regions, and is roughly outlined by boxes in Figures 11-51, which show the amino acid sequences and aligned WD-40 repeats of various WD-40 repeat-containing proteins. Within the 25 central region, peptides should be selected from sequences that have little or no homology to any other known sequences, save the sequence(s) of the protein(s) targeted for disruption.

For example, peptides rIII (SEQ ID NO:4, seven amino acids) and rVI (SEQ ID NO:7, eight amino acids), are identical to segments of RACK1 WD-40 repeats (III and VI, respectively) beginning five amino acids in from the amino termini of the WD-40 repeats from which they are derived (see Fig 1C, underlined segments). The WD-40 repeat segments corresponding to the binding peptides comprise the left portion of the central region of the respective WD-40 repeats, and are not well-conserved in RACK1.

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If it is desired to inhibit the interactions of, for example, all of the isoforms of a particular WD-40-containing protein family, a sequences is selected that includes a significant number of residues that are shared or highly homologous among at least one WD-40 repeat of each of the targeted isoforms.

If, on the other hand, an isoform-specific reagent is desired, a sequence is selected from a WD-40 repeat(s) of a specific isoform, where that sequence does not include a significant number of residues that are identical or highly homologous to residues in WD-40 sequences from related isoforms.

B. Choosing an appropriate length for a peptide.

Effective binding peptides may be designed that range in length from as few as about four residues to 40 or more

15 residues. Preferably, binding peptides will have a length of at least about six residues, and less than about 20 residues. The length will be determined in part by the degree of desired homology to other WD-40 repeats, as described in part A above, and by the level of discrimination between proteins that is

For example, binding peptides selected from RACK1 sequences to inhibit RACK1/PKC interactions were seven and eight amino acids in length. The peptides are long enough to bind specifically to the targeted sequences, but short enough to not cross-react with other WD-40 repeat binding proteins. These properties enable the peptides to have very selective and specific effects, as is shown below in Examples 6-11.

C. <u>Design of RACK1 WD-40-derived peptides to inhibit</u>

RACK1-PKC interactions.

Peptides rIII (SEQ ID NO:4, seven amino acids) and rVI (SEQ ID NO:7, eight amino acids) were designed in part following the guidance presented in parts A and B above. The peptides are identical to segments of RACK1 WD-40 repeat sequences beginning five amino acids in from the amino termini of the WD-40 repeats from which they are derived. The WD-40 repeat segments corresponding to the binding peptides comprise the left portion

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of the central region of the WD-40 repeats. The peptides were tested for their ability to disrupt protein-protein interactions in vitro and in vivo, as described in section VII and Examples 6-11 below.

D. Peptides derived from WD-40 repeats of Human G-Beta inhibit interactions of G-Beta subunits with βARK.

Methods described in section V part E were used to identify WD-40 repeats (SEQ ID NO:128-134) in Human G-Beta (SEQ ID NO:41). Segments from the first six WD-40 repeats were selected for the design of G-beta binding peptides (SEQ ID NO:13-18). The segments were selected based on criteria detailed in parts A and B, above.

The G-beta binding peptides are used to disrupt the interactions of G-beta subunits with βARK . The disruption is assayed using a modification of the overlay assay described in Example 4.

VII. Testing of Putative Binding Peptides.

VII. Testing of Putative Difference of WII. Testing of Putative Detailed below are several assays by which the efficacy of WID-40-derived peptides at binding to a target protein, inhibiting protein-protein interactions, and altering or modulating the activity of a target protein may be determined.

One class of assays, widely-used to assess the binding of two proteins to each other, are overlay assays. Overlay of two proteins to each other, are overlay assays. They can be assays are generally applicable to most proteins. They can be used to, for example, assess the binding of WD-40-derived peptides to their targets, as shown in Example 6 and described peptides to their targets, as shown in Example 6 and described in part B below. Overlay assays can also be used to assess the ability of WD-40-derived peptides to inhibit the binding of two interacting proteins, one of which contains a WD-40 motif from which the peptides were derived (see, for instance, Example 4 and part C below).

Other assays may be used to assess effects of WD-40-derived peptides on the activity of the target protein. These assays may be in vivo assays, in vitro assays, or a combination of in vivo and in vitro assays. The assay used will depend on

the proteins involved and on the system(s) and/or process(es) that involve the interacting proteins against which the peptide was targeted. For instance, the assays described in parts D-I below are appropriate for characterizing PKC activity in vivo and in vitro.

While many of the assays below are particularly useful for characterizing the activity of PKC, they also illustrate a general framework of experiments by which the effects of WD-40 derived peptides on other proteins may be assessed.

A. Overlay assays to evaluate efficacy of putative binding peptides derived from WD-40 regions.

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An overlay assay can be used to assess the disruption of the ability of a pair of proteins to associate. Methods for conducting overlay assays are well-known in the art (see, for example, Mochly-Rosen, et al., 1991).

Applications of overlay assays to evaluate putative binding peptides for PKC/RACK1 interactions are presented in Examples 4 and 5 herein. The assays can be generally described as follows.

One protein of a pair of interacting proteins

("immobilized" protein) can be resolved on an SDS/PAGE gel and blotted onto an appropriate membrane (for example, nitrocellulose or nylon) by methods known to those skilled in the art. The blots may then be contacted with a solution

25 containing the other protein of the pair of interacting proteins ("overlay" protein) in the presence, and in the absence of putative binding peptides. Following appropriate wash steps, bound overlay protein can be detected by the use of an appropriate probe, such as an antibody directed against the

A variation on the above protocol may be performed to minimize a possible interference between unbound binding peptide and antibodies used to detect the presence of bound overlay protein. The modification consists of performing another SDS/PAGE electrophoresis between the steps of binding the overlay protein, and detecting the overlay protein with antibody or other probe. It is accomplished by cutting the blot into

pieces sized to just encompass the area occupied by the blotted immobilized protein, after the overlay protein had been contacted (in the presence or in the absence of binding peptides) and allowed to bind to the blot. The pieces of 5 membrane are then incubated in a sample buffer, placed in the wells of a second SDS polyacrylamide gel and subjected to electrophoresis.

Following electrophoresis, the gel is blotted as above, and contacted with a probe, for example antibodies, to 10 detect bound overlay protein.

Binding of β PKC to peptides homologous to a WD-40 в. region of RACK1.

The binding of β PKC to peptide I (SEQ ID NO:1), peptide rVI (SEQ ID NO:7) and control peptide (SEQ ID NO:9) was 15 assessed in Example 6 using a PKC overlay assay similar to that described in Example 3. Increasing amounts of peptides were applied onto nitrocellulose using a slot-blot apparatus. The membranes were incubated with PKC in the presence and absence of PS, DG, and calcium.

The data are shown in Figure 4, and show that activated PKC bound to both peptides I and rVI at peptide amounts as low as 5 μ moles, but not to the control peptide. Unactivated PKC did not bind to peptide I, but did bind to peptide rVI at similar concentrations.

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The results indicate that while the peptides were homologous to one another and were capable of binding to the same protein, they behaved differently. Peptide rVI (SEQ ID NO:7; 8 residues) was able to bind to both activated as well as unactivated forms of PKC, whereas peptide I (SEQ ID NO:1; 15 30 residues) could bind only to activated PKC. The differences between the binding properties may be due, for example, to charge differences and/or length differences between the two peptides.

C. Effects of peptides homologous to WD-40 region of RACK1 on PKC binding to RACK1

Two peptides (peptide rIII; SEQ ID NO:4 and peptide rVI; SEQ ID NO:7) identical to regions of RACK1 WD-40 repeats (underlined, Figure 1C) were tested for their ability to inhibit PKC binding to recombinant RACK1 using a modification of the overlay procedure referred to above. The experiment is detailed in Example 4 and the results are shown in Figure 3.

Peptide I caused an 81±6% inhibition of PKC binding to recombinant RACK1 as compared with binding in the absence of added peptide. Both peptides rIII and rVI inhibited the binding of PKC to RACK1. In addition, peptides rI and rII were also effective inhibitors of the interaction of PKC to RACK1. A lesser inhibitory effect was obtained with peptides rIV and rV and no inhibition was obtained with peptide rVII.

The difference in the peptide's ability to inhibit binding may reflect differences in the roles played by the corresponding WD-40 repeats in the protein-protein interactions between PKC and RACK1. The peptide's ability or inability to inhibit protein-protein interactions as assayed by an overlay assay, however, is not necessarily correlated with the effects those peptides may have on the activity of the targeted proteins, as measured by both in vivo and in vitro assays and described in parts D-I below.

D. <u>Effects of peptides homologous to WD-40 regions of RACK1 on PKC-mediated oocyte maturation.</u>

Peptides I (SEQ ID NO:1), rIII (SEQ ID NO:4) and rVI (SEQ ID NO:7) were also tested for their ability to affect insulin-induced, PKC-mediated maturation in *Xenopus* oocytes, as detailed in Example 7 and shown in Figures 5A and 5C.

PKC is involved in the maturation of *Xenopus* oocytes. Phorbol esters, which activate PKC, or microinjection of a constitutively active mutant of PKC induce the first stage of oocyte maturation in the absence of hormones. Exposure to insulin causes an increase in diacylglycerol levels and microinjection of activated PKC enhances insulin-induced maturation (Stith, et al.). Microinjection of purified RACK

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proteins causes a significant decrease in the rate of oocyte maturation (Smith, et al., 1992). The insulin-induced oocyte maturation assay therefore provides an effective in vivo assay for compounds that interfere with the function of PKC.

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The maturation response was quantified by monitoring the appearance of a white spot in the animal hemisphere of the oocyte, indicating germinal vesicle breakdown (GVBD) and maturation. The indicated peptides were microinjected into Xenopus oocytes and the percent of oocytes with GVBD following 10 insulin exposure was plotted as a function of time in Figures 5A and C.

Approximately 80-85% of sham-injected (control) oocytes exposed to insulin reach maturation, as compared with 45-50% of oocytes injected with peptide I. The rate of 15 maturation of those oocytes that did mature was similar in the two cases. In contrast the effects of peptide I, both peptides rIII and rVI potentiated the effects of insulin on oocyte maturation, both in terms of the rate of maturation, and in the total fraction of oocytes that mature during the experiment. Injection of peptides rIII or rVI increases the fraction of maturing oocytes to essentially 100%. Furthermore, peptide rVI 20 induced oocyte maturation in the absence of insulin stimulation (Fig. 5B).

Together, the data above indicate that peptides 25 homologous to the WD-40 region of RACK1 can modulate the function of a protein with which RACK1 interacts (e.g. PKC), that the modulation can occur in vivo, and that it can have clear and profound physiological consequences. Furthermore, the results with peptide rVI suggest that under appropriate 30 circumstances, the peptide alone may act to activate PKC, in the absence of other activating substances.

> Effects of peptides homologous to WD-40 regions of E. RACK1 on PKC translocation in Xenopus oocytes. Insulin causes the redistribution of β PKC, but not

35 other PKC isozymes, from a cytosolic form to a membraneassociated form, as evidenced by the relative levels of PKC in the soluble vs. the particulate fraction of oocyte homogenate.

To assess the effects of RACK1 WD-40-derived peptides on insulin-induced PKC translocation, 50 nl of a 20 mM NaCl solution containing the indicated peptides were microinjected into Xenopus oocytes. The oocytes were then homogenized, and the relative amount of PKC in the soluble and particulate fractions was assayed. The protocol followed was a modification of a method described by Smith, et al (1992). The results are shown in Figure 6.

Peptide I (50 μ M) did not affect β PKC distribution in untreated oocytes, but inhibited insulin-induced β PKC translocation (Fig. 3, lanes 7,8). In contrast, peptide rVI (50 μ M) induced β PKC translocation in the absence of insulin treatment (Fig. 3, lanes 3,4). These results suggest that peptide I is an antagonist of hormone-induced PKC translocation, whereas peptide rVI is an agonist and an activator of PKC translocation. In light of the results presented in Example 7, the data also suggest that the inhibition of insulin-induced GVBD following microinjection of peptide I was due to an inhibition of β PKC translocation.

F. Effects of peptides homologous to WD-40 regions of RACK1 on sensitivity of β PKC to Arg-C endopeptidase.

Upon activation of PKC, a pseudosubstrate autoinhibitory sequence at the N-terminus of PKC dissociates from the catalytic site and renders the molecule sensitive to endopeptidase Arg-C (Orr, et al.). Exposure of activated β PKC to Arg-C results in a limited proteolysis, or "nicking" of the enzyme. The nicking typically generates a 78 kDa fragment and several small fragments. Continued exposure to Arg-C typically results in the disappearance of β PKC (Orr, et al.).

Since peptides rIII (SEQ ID NO:4) and rVI (SEQ ID NO:7) exhibited PKC agonist activities in other assays (see, for instance Examples 7 and 8), experiments were performed to determine whether the peptides were capable of activating PKC in a manner to make it susceptible to endopeptidase Arg-C. The experiments are detailed in Example 9 and the results are shown in Figure 7.

In the presence of effective concentrations of PKC activators (0.8 $\mu g/ml$ DG, 50 $\mu g/ml$ PS and 1 mM CaCl₂), exposure of $oldsymbol{eta}$ PKC to Arg-C resulted in nicking, generating the 78 kDa fragment (Fig. 7, lane 2). In the absence of PKC activators, exposure of etaPKC (80 kDa) to endopeptidase Arg-C had no effect on the enzyme (Fig 7, lane 1).

Incubation of etaPKC with Arg-C at low concentrations of activators (2.5 $\mu \mathrm{g/ml}$ PS and 50 $\mu \mathrm{M}$ CaCl₂) in the absence of added peptide, in the presence of control peptide (SEQ ID NO:9) and in the presence of peptide I (SEQ ID NO:1) did not result in appreciable nicking activity (Fig. 7, lanes 4, 8 and 9, respectively). However, incubation of β PKC with the same low concentration of activators in the presence of peptides rIII or rVI resulted in the appearance of the 78 kDa nicked PKC fragment 15 (effects of peptide rVI in Fig. 4, lanes 5-7). Concentrations as low as 10 nM of peptide rVI were sufficient to result in nicking activity, indicative of β PKC activation.

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The results indicate that peptides rIII and rVI, but not peptide I, are effective to stabilize PKC in an activated 20 conformation that renders it susceptible to Arg-C under conditions of low PKC activators that would otherwise not render the enzyme susceptible to Arg-C.

Effects of peptides homologous to WD-40 regions of G. RACK1 on β PKC autophosphorylation.

Activated PKC is capable of autophosphorylation, which can be assayed by incubation with $[\gamma^{-32}P]$ ATP and visualized on an autoradiograph of a gel. Anti-pseudosubstrate antibodies were shown previously to induce autophosphorylation in the absence of PKC activators (Makowske, et al.). Since peptide rVI (SEQ ID NO:7) was effective to induce PKC translocation and GVBD in the 30 absence of PKC activators, experiments were performed to determine if the peptide was also capable of inducing PKC autophosphorylation. The experiments are detailed in Example 10 and the data are shown in Figure 8.

PKC activated with PS (50 μ g/ml), DG (0.8 μ g/ml) and $CaCl_2$ (1 mM) shows normal levels of autophosphorylation (lane 1). No autophosphorylation was seen in the absence of PKC activators

(lane 2), or in the absence of PKC activators with peptide I (SEQ ID NO:1; lane 5) or control peptide (SEQ ID NO:9; lane 6). In contrast, peptide rVI in the absence of PKC activators induced PKC autophosphorylation to over 80% of the levels 5 obtained for PKC alone in the presence of optimal concentration of PS, DG, and calcium (compare Fig. 8 lane 1 (control) with lane 4 (peptide rVI)).

Effects of peptides homologous to WD-40 regions of H. RACK1 on histone phosphorylation by β PKC.

10 Another measure of PKC activity is the ability of activated PKC enzyme to phosphorylate histones. PKC phosphorylation of histone was carried out using a modification of the protocol described by Mochly-Rosen, et al., (1987). Phosphorylation was carried out in the presence or absence of 15 PKC activators (PS, DG and calcium) and RACK1-derived peptides. Phosphorylated histone was detected by autoradiography, following SDS-PAGE on a 10% gel.

Since peptide rVI (SEQ ID NO:7) was effective to induce the autophosphorylation of PKC in the absence of PKC activators, and both peptides rIII (SEQ ID NO:4) and rVI 20 rendered PKC susceptible to proteolysis by Arg-C, experiments were performed to characterize the effect of the peptides on histone type III phosphorylation by PKC. The experiments are detailed in Example 11 and the results are shown in Figures 9 and 10.

The results are similar to those obtained for the effects of peptide rVI on autophosphorylation of PKC, that is, peptide rVI was effective to induce PKC-mediated histone phosphorylation in the absence of the PKC activators PS, DG, and 30 calcium, once again supporting that peptide rVI is an agonist of PKC activation. Peptide rIII similarly induced histone phosphorylation (Fig. 10).

VIII. <u>Utility.</u>

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Peptides as probes for the identification of target proteins.

WD-40 derived peptides may be used, for example, to 5 isolate clones encoding target proteins from an expression library. Variations on the cloning methods described herein can be used to identify clones expressing sequences capable of binding the peptides. For example, WD-40 derived peptides may be used to detect a target protein on a membrane using a 10 standard binding assay. Positive clones may be detected, for example, by radiolabeling the peptides and exposing the membrane to film.

Target proteins isolated in this manner may be completely novel, or they may be partially characterized (in 15 terms of a biological activity in a homogenate, or a band on a protein gel, for example).

Upon isolation of a cDNA encoding a binding protein, the cDNA may be expressed, for example, as detailed herein, and the protein may be characterized. Purified protein thus isolated may be used for a number of applications, including the production of antibodies.

Peptides designed according a method of the present invention may also be used, for example, as probes in a Western blot of a tissue homogenate to identify and determine the molecular weight of known or putative target proteins.

Screens such as those described above may be facilitated by the modification of peptides used for screening to incorporate any of a variety of reporter moieties. For example, the peptides can be radiolabeled with 125I.

Alternatively, the peptides can be modified with a sequence-tag or a ligand for an affinity column by methods known to those skilled in the art.

The peptides may also be modified to covalently crosslink to their targets after binding, for example with any of 35 various affinity reagent for cross linking known to those skilled in the art. This enables the isolation of target proteins that bind the peptides relatively weakly.

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B. <u>Peptides as substitutes for defective WD-40 containing proteins.</u>

In cases where a WD-40 containing protein is implicated in a disease (see, for example Reiner, et al.), peptides derived from WD-40 regions of the defective protein may be used as substitutes, for example, to activate a target enzyme. Such an approach may be more feasible than attempting therapy with intact proteins. The approach has an additional advantage in that it does not require knowledge of the chromosomal location of the affected gene.

The peptides can be introduced into affected cells by any of several methods known to those skilled in the art, including through the use of an appropriate expression vector or through *in vitro* synthesis and administration by an effective, expedient route. In vitro studies can be carried out using skinning or microinjection techniques.

C. <u>Peptides as pharmaceutical agents.</u>

WD-40 derived peptides of the present invention may be used therapeutically, as described above. Such peptides may be designed so as to interact with endogenous target molecules to augment or correct their function. Alternatively, peptides may be designed to specifically interact with target molecules unique to a pathogenic organism.

D. <u>Peptides as modulators of enzyme activity of proteins</u> involved in protein-protein interactions.

Peptides synthesized according to a method of the invention may be effective to modulate the function of a target molecule (e.g. serve as agonists or antagonists). As shown herein, for example, peptides rVIII and rVI can serve to activate or enhance the activation of PKC, whereas peptide I can inhibit PKC.

These activities may be used in screens to identify other compounds which may affect the function of target molecules such as PKC. In particular, because WD-40 derived peptides may interact with PKC in a manner that is more similar to in vivo interactions (i.e. protein binding), they may be

useful for identifying molecules or compounds that may interfere with PKC function in vivo, but might not necessarily interfere with PKC in vitro.

For example, peptide rVI can be used to stimulate PKC 5 in the absence of traditional PKC activators, and the rVIstimulated enzyme may be used in a screen to identify, for example, novel PKC-inhibiting or PKC-potentiating compounds.

If constitutive activation or inactivation of a target enzyme is desired, peptides may be designed with integrated or 10 derivatized cross-linking moieties. The peptides can be crosslinked to their targets upon binding such that the target molecule assumes the desired state of activity for the lifetime of the target molecule.

Conversely, as described herein for PKC, peptides may 15 also be designed so as to accelerate the degradation of the target molecule. For example, peptide rIII accelerated the degradation of PKC in cardiac myocytes.

WD-40 derived peptides as specific modulators of E. isozymes.

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Peptides designed according to a method of the present invention can also be used to provide target isozyme-specific modulator molecules. For example, most cells have several PKC isozymes, all of which are activated by the same cellular stimuli. Determining the function of the individual isozymes is therefore difficult. 25

WD-40 derived peptides that selectively stimulate or inhibit specific target isozymes or groups of isozymes may be useful, both in terms of therapeutic value, and in terms of determining the roles of different isozymes in cellular function 30 and disease. Such information can be useful for the identification of new molecular targets for drug development, as is described in part F, below.

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F. <u>Compounds designed based on the predicted structure of binding peptides as pharmaceutical agents.</u>

Peptides derived from WD-40 repeats may be useful for identifying lead compounds for drug development. Peptides as small as 7 residues have been shown herein to possess specific bioactivities upon interaction with their targets in vivo. The structure of such small peptides can be readily determined by a number of methods, such as NMR and X-ray crystallography. A comparison of the structures of peptides similar in sequence, but differing in the biological activities they elicit in the target molecules, can provide information about the structure-activity relationship (SAR) of the target enzyme.

For example, peptide I and RACK1-derived peptides rIII (SEQ ID NO:4) and rVI (SEQ ID NO:7) had opposite effect in vivo, although they are homologous in sequence.

Information gleaned from the examination of structure-activity relationships can be used to design either modified peptides, or other small molecules or lead compounds which can be tested for predicted properties (e.g. agonist or antagonist), as related to the target enzyme. The activity of the lead compounds can be evaluated using assays similar to those used in the evaluation of peptide-binding effects.

Information relating to a SAR of a target enzyme may also be obtained from co-crystallization studies. In such studies, a peptide with a desired activity is crystallized in association with a target protein, and the X-ray structure of the complex is determined. The structure can then be compared, for example, to the structure of the target protein in its native state, and information from such a comparison may be used to design compounds expected to possess specific activities. The compounds can be evaluated using assays similar to those used in the evaluation of peptide-binding effects.

G. PCR of cDNA corresponding to WD-40 repeats to identify mutations in WD-40 containing proteins.

Results presented herein suggest that the middle regions of WD-40 motifs are involved in the association of a WD-40 protein with its target protein. Because this association

is likely to play a central role in the activity of a polypeptide complex comprised of interacting proteins, some genetic diseases may include mutations at these regions of WD-40 Therefore, if a WD-40 containing 5 protein is implicated in a genetic disorder, it may be possible containing proteins. to use PCR to amplify DNA from the WD-40 regions to quickly check if a mutation is contained within one of the WD-40 motifs. Primers can be made corresponding to either (i) the flanking regions of each repeat or (ii) the flanking regions of a series 10 of tandem repeats from the affected gene. Standard sequencing techniques can be used to determine whether a mutation is present. This method does not require prior chromosome mapping of the affected gene and can save time by obviating the need to sequence the entire gene encoding a defective WD-40 protein.

WD-40 based polypeptides as affinity ligands

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Since the polypeptide compositions of the invention Η. are able to bind proteins of interest, generically called a "first protein", the polypeptide compositions can also be used to retrieve the proteins of interest from samples and the 20 peptides can be used as affinity ligands for chromatographic procedures to purify and analyze said proteins. chromatographic techniques are employed. Typically, the polypeptide is coupled to a solid support and the sample putatively containing the first protein is contacted with the 25 polypeptide composition of the invention; any unbound components of the sample are removed and, if desired, the first protein, bound to support, is eluted and recovered.

> Use of peptides in screening tests for candidates I. Various candidate compounds, not necessarily

polypeptides, may be shown to bind to a first protein using the polypeptides of the invention as competitors. In these screening assays, the ability of a candidate compound to bind a first protein can be assessed by contacting the first protein with the polypeptide composition of the invention in the 35 presence and absence of the candidate compound and evaluating the level of binding of the polypeptide in the presence as opposed to the absence of the candidate. Decreased binding of

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the polypeptide in the presence of the candidate indicates that the candidate binds to the first protein.

More broadly, the interaction of a protein with a polypeptide subsequence contained in the second protein can be assessed by contacting the first protein with a polypeptide representing the subsequence and observing any interaction with the polypeptide composition.

IX. Production of the Peptides of the Invention

The polypeptides of the invention can be prepared using standard techniques for the synthesis of peptides from amino acids. Such techniques, when conducted in solid phase chemistry are available commercially.

The polypeptides of the invention may also be produced using recombinant methods. These methods are by now well known in the art; DNA molecules containing nucleotide sequences encoding the desired polypeptides can readily be synthesized and ligated into expression systems for production of the peptides as is understood in the art. A wide variety of hosts is available, including procaryotic and eucuryatic hosts. The construction of expression vectors, means to modify these hosts, and culturing the modified hosts for recombinant production of polypeptides are conducted using standard techniques.

The following examples illustrate, but do not limit the present invention.

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Materials and Methods

Nitrocellulose filters were obtained from Schleicher and Schuell (Keene, NH).

Synthetic peptides were prepared using commercially available automated peptide synthesizers. Alternatively, custom designed peptides may be purchased, for example, from Bachem Bioscience (King of Prussia, PA). Peptides may also be prepared recombinantly by expressing oligonucleotide sequences encoding the peptides. The oligonucleotide sequences may be either synthesized directly by standard methods of oligonucleotide synthesis, or, in the case of large coding sequences, synthesized by a series of cloning steps involving a tandem array of multiple oligonucleotide

fragments corresponding to the coding sequence (Crea; Yoshio, et al.; Eaton, et al.). Oligonucleotide coding sequences can be expressed by standard recombinant procedures (Maniatis, et al.; Ausubel, et al.).

"Triton" refers to a nonionic detergent comprising a polyoxyethylene ether and other surface-active compounds. exemplary Triton detergent is "TRITON X-100", available from Sigma Chemical Company, St. Louis, MO.

"Tween" refers to a nonionic detergent comprising 10 polyoxyethylenesorbitan monolaurate with a fatty acid composition of approximately 55% lauric acid, with a balance composed primarily of myristic, palmitic and stearic acids. An exemplary Tween detergent is "TWEEN 20", available from Sigma Chemical Company, St. Louis, MO.

"SDS" refers to sodium dodecyl sulfate. 15

"PAGE" refers to polyacrylamide gel electrophoresis.

"IPTG" refers to isopropyl &-D-thiogalactopyranoside.

Example 1

Expression Cloning of a PKC-binding Protein

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Overlay block buffer: 50 mM Tris-HCl (pH 7.5), 0.2 M Buffers. NaCl, 3% bovine serum albumin (BSA) and 0.1% polyethylene glycol. Overlay buffer: 50 mM Tris-HCl (pH 7.5), 0.2 M NaCl, 12 mM 2-mercaptoethanol, 0.1 % BSA, 1% polyethylene glycol, $10\mu g$ per 25 ml soybean trypsin inhibitor and $10\mu g$ per ml leupeptin.

Isolation of a PKC-binding cDNA clone by an overlay в.

A rat brain (Sprague Dawley) cDNA expression library, constructed in the lambda phage cloning vector "UNI-ZAP XR" 30 (Stratagene, La Jolla, CA), was screened by an overlay assay as follows.

Lifts of nitrocellulose filters from IPTG-induced cDNA library plates were incubated for 2 hours in overlay block buffer. The filters were then transferred to overlay buffer with or without 1 unit of a mixture of rat brain PKC isozymes (α , β , γ , δ , ϵ and ζ , ~10 nM final concentration each) and incubated for 20 minutes

at room temperature with PKC activators (60 μ g/ml phosphatidylserine (PS), 2 μ g/ml diacylglycerol (DG), 1 mM CaCl₂).

Following three 15 minute washes in the overlay buffer, the filters were incubated in the overlay block buffer in the presence of a mixture of monoclonal anti- α , β and γ PKC antibodies (1:1000 dilution; Seikagaku Kogyo, Tokyo, Japan) and polyclonal anti- δ , ϵ and ζ PKC antibodies (1:500 dilution; Life Technologies, Gaithersburg, MD). After a 16 hr incubation at room temperature, the filters were washed three times, 15 minutes per wash, in overlay buffer.

Binding of PKC was determined using alkaline phosphatase-conjugated goat anti-rabbit or goat anti-mouse antibodies (1:2000 dilution, Boehringer Mannheim Biochemicals, Indianapolis, IN). The alkaline phosphatase reaction used 5-bromo-4-chloro-3-indoyl phosphate p-toluidine salt as a substrate, and was performed following the manufacturer's protocol.

Library screening of 2.4 x 10⁶ recombinant "UNI-ZAP" lambda phage plaques yielded one clone, pRACK1, that reacted with anti-PKC antibodies in the PKC overlay membrane, but not in the control overlay membrane. These results suggest that pRACK1 encodes a PKC binding protein.

C. Cloning and sequencing cDNA from positive plaques.

The clone pRACK1, identified as detailed in part B above, was plaque purified and cDNA inserts were isolated as phagemids by in vivo excision of the cloning vector, according to the manufacture's protocol (Stratagene, La Jolla, CA). DNA sequencing of pRACK1 was carried out using standard di-deoxy sequencing techniques (Maniatis, et al.) The DNA sequence of RACK1 is shown in Figure 1A. The sequence is also contained in the Sequence 30 Listing as SEQ ID NO:19.

Example 2

Expression and Purification of Recombinant RACK1 Protein in E. coli

A PstI/XhoI DNA fragment containing an open reading frame 35 of 317 amino acids from the putative translation start site of pRACK1 (see underlined ATG in Fig. 1A) and 8 additional nucleotides

upstream of the initiating methionine was subcloned into $E.\ coli$ expression vector pMAL-c2 (New England BioLabs, Beverly, MA). This vector contains the malE gene, which encodes maltose-binding protein (MBP). Induction of E. coli containing the vector results 5 in the production of an MBP-fusion protein (Ausubel, et al.). vector also includes a recognition site for the protease factor Xa, which allows the protein of interest to be cleaved from MBP after purification without adding any vector-derived residues to the protein.

A culture of TB1 E. coli transformed with RACK1containing pMAL-c2 was induced by a 3 hr incubation with 1.8 mM A protein fraction containing a 78 kDa fusion protein, comprised of RACK1 fused to MBP was isolated from the cultured E. The fusion protein was coli by standard methods (Ausubel). an amylose affinity column according 15 purified on manufacture's protocol (New England BioLabs, Beverly, MA) and incubated with protease Xa (New England BioLabs) to yield a 36 kDa protein (RACK1) and a 34 kDa protein (possibly a RACK1 degradation product).

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Example 3

Binding of PKC to Recombinant RACK1

Buffers. Α.

PBS/Tween buffer: 140 mM NaCl, 8 mM Na₂PO₄, 1.5 mM KH₂PO₄, 3 mM-KCl and 0.05% Tween at pH 7.0.

Overlay wash buffer: 50 mM Tris-HCl (pH 7.5), 0.2 M NaCl, 12 mM 2-mercaptoethanol, 0.1% polyethylene glycol and 0.1 mM CaCl $_2$.

Overlay assay. в.

Purified recombinant RACK1 protein (100-250 μg per lane, produced as detailed in Example 2) was subjected to SDS/PAGE and (Ausubel). membranes nitrocellulose 30 blotted onto nitrocellulose membranes were cut into strips, which were incubated for 0.5 hr in overlay buffer (Example 1) in the presence or absence of a mixture of PKC isozymes (α , β , γ , δ , ϵ and ζ , ~10 nM each (60 activators PKC concentration) and 35 phosphatidylserine (PS), 2 $\mu g/ml$ diacylglycerol (DG), and 1 mM $CaCl_2$). Unbound material was removed by five washes, 5-min each,

in overlay wash buffer. Where indicated, PKC activators were present during the incubation of PKC with the nitrocellulose strips. The conditions for each sample and corresponding results are presented in part D below.

C. <u>Detection of bound PKC.</u>

PKC bound to RACK1 immobilized on nitrocellulose strips was detected as follows. The strips were incubated for 16 hours at room temperature with a mixture of anti-PKC antibodies as detailed in part B of Example 1, and then washed three times, 15 10 minutes per wash, with PBS/Tween buffer. The strips were incubated with anti-mouse and anti-rabbit horseradish secondary antibodies (Amersham Life Science, Arlington Heights, IL) peroxidase-linked diluted 1:1000 in PBS/Tween buffer supplements with 2% BSA, for 1 hour at room temperature. After washing three times, 15 minutes 15 per wash with PBS/Tween buffer, the strips were subjected to a chemiluminescent reaction with luminol (diacylhydrazide) as detailed in the maufacturer's protocol (Amersham Life Science, Arlington Heights, IL), followed by an immediate exposure to autoradiography film (Eastman Kodak, Rochester, NY) for 30 seconds 20 to 5 minutes.

D. Effects of PKC activation on PKC binding to RACK1.

The results presented in Figure 2 show the influence of PKC activators on the binding of PKC to RACK1 immobilized on nitrocellulose membranes. The overlay assay was carried out as described in part B above. The test reagents contained in each sample and the corresponding lanes on the blot presented in Fig. 2 are as follows. Lane 1: PKC, 60 µg/ml PS, 2 µg/ml DG and 1 mM CaCl₂; lane 2: PKC and 1 mM EGTA; lane 3: PKC, 60 µg/ml PS and 2 µg/ml DG; lane 4: PKC and 1 mM CaCl₂; lane 5: No PKC added; lanes 6 and 7: PKC, 60 µg/ml PS 2 µg/ml DG, 1 mM CaCl₂, and 10 µM substrate peptide (SEQ ID NO:11; lane 6) or 10 µM pseudosubstrate peptide (SEQ ID NO:12; lane 7). The results are representative of three independent experiments.

It can be appreciated that the binding of PKC as detected by anti-PKC antibodies is minimal in the presence of EGTA or calcium alone (Fig. 2, lanes 2, 4, respectively), is greater in the

presence of phosphatidylserine (PS) and diacylglycerol (DG; lane 3), and is maximal in the presence PS, DG and calcium (lane 1). Antibody binding was not observed in the absence of added PKC (lane 5). Furthermore, maltose binding protein alone, or an extract from 5 non-transformed E. coli did not bind PKC.

The concentration dependence of PKC binding to RACK1 was characterized with etaPKC, since this isozyme is a major component of the PKC mixture used for the overlay assay. The mean half maximal binding was ~ 0.375 nM, and maximal binding was ~ 4 nM (n=3; values reflect binding of etaPKC isozyme in the presence of other PKC isozymes and was determined by scanning autoradiograms in the linear range of detection, as described in Mochly-Rosen, et al., (1991).

The results presented above indicate that in order for 15 PKC to bind to RACK1 it must be activated. In vitro, activation may be accomplished, for example, by phosphatidylserine and diacylglycerol, or, more preferably, by phosphatidylserine, diacylglycerol and calcium.

Example 4

Inhibition of PKC Binding to RACK1 by RACK1-specific WD-40homologous Peptides 20

Assays for the inhibition of PKC binding to RACK1 by putative binding peptides were carried out by combining a variation of the overlay protocol described in Example 3 part B above, with 25 an overlay extraction assay described in part B below. variation in the overlay protocol consisted of incubating the putative binding peptides with a mixture of PKC isozymes for 15 minutes at room temperature before the mixture was used to contact the nitrocellulose strips containing immobilized RACK1.

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Sample buffer: 0.3 M Tris HCl, 5% SDS, 50% glycerol, Buffers. 0.01% bromophenol blue and 5% β -mercaptoethanol.

B. Overlay extraction protocol.

Nitrocellulose strips containing immobilized RACK1, that had been contacted with a solution containing a mixture of PKC isozymes, were washed and the area corresponding to the 36 kDa (RACK1-containing) band was cut out. The pieces (containing PKC/RACK1 complexes) were incubated with sample buffer for 10 minutes at 80°C. The sample buffer and the nitrocellulose pieces were then placed in wells in the PAGE gel and subjected to SDS-PAGE to elute the bound proteins. The gel was blotted onto nitrocellulose and a Western blot analysis was carried out using the mixture of antibodies (specific for PKC α , β , γ , δ , ϵ and ζ isozymes) described in Example 1 part B. Bound antibodies were detected by $^{125}\text{I-protein A}$.

C. PKC overlay in the presence of binding peptides.

Peptides derived from or homologous to WD-40 repeats of RACK1 were tested for their ability to inhibit PKC binding to recombinant RACK1. Binding of PKC to RACK1 was carried out using a variation of the overlay procedure described in Example 3 part B. In the experimental samples, peptides were incubated with a solution containing a mixture of rat brain PKC isozymes (~10 nM each) for 15 minutes at room temperature.

Following completion of the modified overlay protocol, the samples were subjected to the overlay-extraction protocol detailed in part B, above.

The results in Figure 3 show the binding of PKC to RACK1, carried out without (lane 1) or with (lanes 2-4) a preincubation of peptides with PKC. Lane 2 shows PKC binding following a preincubation with 10 μM peptide I (SEQ ID NO:1). Peptide I caused an 81±6% inhibition of PKC binding to recombinant RACK1 as compared with binding in the absence of added peptide (n=3). Lanes 3 and 4 show PKC binding following a preincubation with 10 μM peptide rIII (SEQ ID NO:4) and 10 μM peptide rVI (SEQ ID NO:7), respectively. Both peptides inhibit the binding of PKC to RACK1. It can be seen that peptide rIII is somewhat more effective than peptide rVI. The results shown are representative of three independent experiments.

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The overlay-extraction method (part B above) was used in experiments relating to the peptide inhibition of PKC binding in order to decrease the possibility that some part of the inhibition of PKC binding to RACK1 reflects an interference in the binding of 5 anti-PKC antibodies to the PKC/RACK1 complexes. Free peptides are effectively removed from the PKC/RACK1 complexes during the second round of SDS/PAGE, prior to blotting and detection of immobilized PKC/RACK1 complexes by anti-PKC antibodies.

Example 5

Identification of Sequenced Proteins Containing WD-40 Repeats 10

A search for WD-40 motif-containing proteins was done using the ENTREZ program, release 6.0 (National Center for Biotechnology Information, National Library of Medicine, National Institutes of Health, Bethesda, MD). The ENTREZ database was 15 searched for protein sequences related to the eta subunit of transducin.

Protein sequences homologous to eta-transducin were examined for the existence of WD-40 repeats, following the guidance for identification of WD-40 repeats presented in section V of the specification, above.

The proteins were also used to carry out additional searches of the database, in order to identify other proteins which may contain WD-40 repeats, but which might not be homologous to the eta subunit of transducin. Sequences identified during the second round of searches were again examined for WD-40 repeats.

This search strategy identified 30 proteins containing WD-40 sequences. The amino acid sequences of these proteins, with the WD-40 regions aligned and delineated, are shown in Figs. 12-18, The sequences are 20-27, 29-30, 34-35, 37-38, 40 and 42-50. represented in the Sequence Listing as SEQ ID NO:29-35, 37-44, 46-47, 51-52, 54-55, 57 and 59-67. An examination of the sequences in the figures reveals that although there can be divergence between the WD-40 motifs of different proteins, a consistent pattern can be inferred based on the teachings presented in part 35 V of the specification above.

An additional search, using a consensus WD-40 sequence (SEQ ID NO:262), was conducted with the "MACVECTOR" program (Eastman Kodak Co., New Haven, CT) to search GenBank (December 1993 release). Default settings (matrix=250) were used for the search. The search identified the 250 proteins with the highest homology to the consensus sequence. These proteins were examined, as detailed in part V above, for WD-40 repeats. Ten additional proteins containing WD-40 repeats were identified with this strategy. The amino acid sequences of those proteins, with the WD-40 repeats aligned and delineated, are shown in Figs. 11, 19, 28, 31-33, 36, 39, 41 and 51. The sequences are represented in the Sequence Listing as SEQ ID NO:28, 36, 45, 48-50, 53, 56, 58 and 68.

Example 6

Binding of β PKC to RACK1 WD-40-derived Peptides

A. <u>Buffers</u>.

Peptide overlay block buffer: 20 mM Tris-HCl (pH 7.5), 0.2 M NaCl, 3% bovine serum albumin (BSA) and 0.1% polyethylene glycol.

Overlay wash buffer: 50 mM Tris-HCl (pH 7.5), 0.2 M NaCl, 12 mM 2-mercaptoethanol, 0.1% polyethylene glycol and 0.1 mM CaCl $_2$.

B. PKC overlay of immobilized peptides.

20 The binding of etaPKC to peptide I (SEQ ID NO:1), peptide rVI (SEQ ID NO:7) and control peptide (SEQ ID NO:9) was assessed using a PKC overlay assay similar to that described in Example 3. Increasing amounts of peptides (0.5 μ mole, 1.0 μ mole, 5.0 μ mole and 10.0 $\mu\text{mole})$ suspended in 20 mM NaCl were applied individually onto nitrocellulose using a slot-blot apparatus (Schleicher and Schuell, 25 Keene, NH). The nitrocellulose membrane was washed three times, 15 minutes per wash, in peptide overlay buffer and incubated for two hours in peptide overlay block buffer. The membrane was cut into sections and the sections were transferred to different PKCcontaining solutions and incubated for 30 minutes at 30 temperature. All the solutions contained 5 nM rat brain PKC in peptide overlay buffer. Some solutions additionally contained PS, DG, and calcium. The membranes were then washed three times, 15 minutes per wash, in peptide overlay buffer and incubated in peptide overlay block buffer containing anti-etaPKC monoclonal 35 antibodies (1:1000 dilution; Seikagaku Kogyo, Tokyo, Japan). After

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a 16 hr incubation at room temperature, the filters were washed three times, 15 minutes per wash, in peptide overlay buffer.

Binding of PKC was determined using chemiluminescence as described in Example 3, part C. Quantitation of PKC binding was 5 carried out using a "MICRO SCAN" 1000 gel analyzer (Galai Inc., Yokneam, Israel).

The data show that activated PKC bound to both peptides I and rVI, but not to the control peptide, at peptide amounts as low as 5 μ moles. Unactivated PKC did not bind to peptide I, but did bind to peptide rVI at similar concentrations.

The results indicate that peptide rVI is capable of binding both activated as well as unactivated forms of PKC, whereas peptide I binds only to activated PKC.

Example 7

Effects of RACK1 WD-40-derived Peptides on PKC-mediated Oocyte 15 <u>Maturation</u>

Exposure to insulin induces maturation in Xenopus oocytes via a PKC-dependent pathway (Smith, et al., 1992). The maturation response may be quantified by monitoring the appearance of a white spot in the animal hemisphere of the oocyte, indicating germinal vesicle breakdown (GVBD) and maturation. To assess the effects of RACK1 WD-40-derived peptides on insulin-induced PKC-mediated maturation, 50 nl of a 20 mM NaCl solution containing the indicated peptides [peptide I (SEQ ID NO:1; ●), peptide rVI (SEQ ID NO:7; ■), 25 or injection solution (\square)] (peptides at 50 μM) were microinjected into Xenopus oocytes. The symbols refer to symbols used in Figure 5, which shows the data from this example. One hour following the peptide injections, the occytes were exposed to a solution containing insulin (8.25 $\mu g/ml$) for 2 minutes (t=0). 10-15 oocytes 30 were used for each sample.

independent representative three of data, The experiments, are expressed as the percent of oocytes with GVBD following insulin exposure and are plotted as a function of time in Figure 5.

In oocytes injected with buffer or control peptide, onset 35 of maturation was typically 4-5 hours after exposure to insulin. Following this delay, %GVBD followed an approximately exponential time-course, reaching a plateau of about 85-90% GVBD at about 10-12 hours. These data indicate that approximately 80-85% of shaminjected oocytes exposed to insulin at t=0 reach maturation, and that maturation is reached relatively quickly (within about 10 hours) relative to the time-course of the experiment (20 hours).

Occytes injected with peptide I (SEQ ID NO:1) responded in a manner similar to control occytes, except the plateau was at about 45-50% GVBD. These data suggest that injection of peptide I blocked maturation in approximately 40-45% of cocytes that would normally proceed to maturation, but had little effect on the kinetics or extent of maturation of the remaining (50-55%) cocytes.

10

Occytes injected with peptide rVI (SEQ ID NO:7) responded with a slightly shorter delay (about 3-4 hours), but reached a higher plateau (about 95-100% GVBD) more quickly (within about 5 hours) than control oocytes. These data suggest that peptide rVI potentiates the effects of insulin on oocyte maturation, both in terms of the rate of maturation, and in the total fraction of oocytes that mature during the experiment. Injection of peptide rVI increases the maturing fraction to essentially 100%

The effects of both peptides I and rVI on GVBD were dosedependent between 5 $\mu\text{m-}500~\mu\text{M}.$

Since peptide rVI enhanced insulin-induced GVBD, experiments were performed to determine whether peptide rVI can induce GVBD in the absence of insulin. The data from these experiments are shown in Fig. 5B. Microinjection of peptide rVI (50 \(\mu\mathbb{M}\mathbb{M}\)) alone, but not peptide I, control peptide or buffer, induced GVBD. Maturation initiated with a longer delay (about 6-7 hours) than in the control insulin-induced oocytes in Fig. 5A (about 4-5 hours), and reached a plateau of about 50% GVBD.

Together, the data above indicate that peptides homologous to the WD-40 region of RACK1 modulate the function of PKC. Peptide I inhibited PKC-mediated oocyte maturation by about 40%, whereas peptide rVI potentiated insulin-induced maturation, and resulted in a limited maturation response even in the absence of insulin. The latter result suggests that peptide rVI, under appropriate circumstances, may act to activate PKC in the absence of other activating substances.

Example 8

Effects of RACK1 WD-40-derived Peptides on PKC Translocation in Xenopus Oocytes

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Homogenization buffer: 20 mM Tris HCl, pH 7.5, 10 mM Α. EGTA, 2 mM EDTA, 0.25M sucrose, $10\,\mu\text{M}$ phenylmethylsulfonyl fluoride, $20\mu g/ml$ of each leupeptin and soybean trypsin inhibitor.

PKC translocation in oocytes.

Insulin causes the translocation of β PKC, but not other 10 PKC isozymes, from a cytosolic form to a membrane-associated form, as evidenced by the relative levels of PKC in the soluble vs. the particulate fraction of oocyte homogenate. To assess the effects insulin-induced WD-40-derived peptides on translocation, 50 nl of a 20 mM NaCl solution containing the indicated peptides were microinjected into Xenopus oocytes. oocytes were then homogenized, and the relative amount of PKC in the soluble and particulate fractions was assayed. The protocol followed was a modification of a method described by Smith, et al. The results are shown in Figure 6.

Batches of 50 oocytes were microinjected with either peptide rVI (SEQ ID NO:7; 50 μ M; lanes 3, 4), peptide I (SEQ ID 20 NO:1; 50 μ M, lanes 7, 8) or injection solution (NaCl 20 mM, lanes Homogenates from each batch were prepared 60 minutes after microinjection (lanes 1-4) or 60 minutes after 25 addition of insulin (lanes 5-8). The homogenates were centrifuged at 10,000 g for 3 minutes, the upper layer (containing fat and yolk) was removed, and the remainder was frozen at -70 °C. Prior to use, the samples were thawed, 200 μl homogenization buffer was added and the samples were centrifuged at 100,000 g for 30 minutes at 4 °C. The supernatants (soluble fraction) were removed and "CENTRICON" 30 using μ l 20 The pellets (particulate fractions) were concentrated to dissolved in 20 μl of homogenization buffer. The samples were (Amicon, Beverly, MA). resolved on an 8% SDS/PAGE gel and blotted onto nitrocellulose. 35 The amount of PKC in each fraction was determined by Western blot using anti-etaPKC antibodies (1:1000 dilution; Seikagaku Kogyo,

Japan). Bound primary antibodies were detected by chemiluminescence as described in Example 3, part C.

The antibodies showed immunoreactivity with an ~80 kDa protein that corresponds to β PKC. Data are representative of three experiments.

The data are shown in Figure 6. Lanes 1, 3, 5 and 7 contain particulate fractions (p), while lanes 2, 4, 6 and 8 contain soluble (cytosol) fractions (c). Peptide I (50 μ M) did not affect etaPKC distribution in untreated oocytes, but inhibited 10 insulin-induced β PKC translocation (Fig. 3, lanes 7,8). contrast, peptide rVI (50 μM) induced βPKC translocation in the absence of insulin treatment (Fig. 3, lanes 3,4).

The results above suggest that peptide I is an antagonist of insulin-induced PKC translocation, whereas peptide rVI is an agonist and an activator of PKC translocation. In light of the 15 results presented in Example 7, the data also suggest that the inhibition of insulin-induced GVBD following microinjection of peptide I was due to an inhibition of β PKC translocation.

Example 9

Effects of RACK1 WD-40-derived Peptides on Sensitivity of PKC to 20 Arg-C Endopeptidase

Α. Buffers.

Sample buffer: 0.3 M Tris HCl, 5% SDS, 50% glycerol, 0.01% bromophenol blue and 5% β -mercaptoethanol.

25 Nicking of β PKC by Arg-C endopeptidase. B.

Upon activation of PKC, a pseudosubstrate autoinhibitory sequence at the N-terminus of the molecule dissociates from the catalytic site and becomes sensitive to endopeptidase Arg-C (Orr, et al.). In the absence of PKC activators, exposure of the 80 kDa etaPKC to endopeptidase Arg-C has no effect on the enzyme (see Fig 7, lane 1). In the presence of the PKC activators PS, DG and calcium, however, exposure of etaPKC to Arg-C results in a "nicking" of the PKC (i.e. limited proteolysis generating a 78 kDa fragment and several small fragments (see Fig. 7, lane 2)). Continued exposure to Arg-C results in the disappearance of etaPKC (Orr, et 35 al.). The present experiment tests whether peptides derived from

the WD-40 region of RACK1 alter the sensitivity of β PKC to endopeptidase Arg-C.

The methods used to assay Arg-C sensitivity are a modification of methods described by Orr, et al. Rat brain PKC (~5 nM) was incubated at room temperature in 500 μl of 20 mM Tris-HCl buffer (pH 7.5) alone or with Arg-C (5 units/ml) in the presence or absence of the indicated peptides (final concentration 10 μM or as indicated), PS, DG, and calcium (as indicated). 50 μl aliquots were removed into 20 μl of sample buffer during the reaction as indicated (samples in all the lanes were incubated for 30 minutes, except lanes 5, and 6, which were incubated for 5 and 15 minutes, except lanes 5, and 6, which were incubated for 10 minutes at 80°C and respectively). The samples were boiled for 10 minutes at 80°C and loaded onto 8% SDS-PAGE. βPKC was detected by Western blot analysis using anti-βPKC antibodies as described in Examples 6 and

The results are shown in Figure 7. PKC was incubated for the indicated time alone (lane 1) or in the presence of Arg-C (lanes 2-9), with DG (0.8 μ g/ml), PS (50 μ g/ml) and CaCl₂ (1 mM; (lane 2), with PS (50 μ g/ml) and CaCl₂ (1 mM; lane 3), with PS (2.5 lane 2), with PS (50 μ g/ml) and CaCl₂ (50 μ M; lane 4); with PS (2.5 μ g/ml), CaCl₂ (50 μ M) and with either peptide rVI (SEQ ID NO:7; 10 μ M; lanes 5-7), and with either peptide rVI (SEQ ID NO:9; lane 8) or with peptide I (SEQ ID NO:1; lane 9).

Incubation of βPKC with Arg-C at low concentrations of activators (2.5 μg/ml PS and 50 μM CaCl₂) in the absence of added peptide did not result in appreciable nicking activity (Fig. 7, lane 4). Similarly, nicking of βPKC did not occur in the presence of this concentration of activators with peptide I (lane 9) or with control peptide (lane 8). However, incubation of βPKC with the same concentration of activators in the presence of peptide rVI resulted in a time-dependent appearance of the 78 kDa nicked PKC fragment (Fig. 4, lanes 5-7). Concentrations as low as 10 nM of peptide rVI were sufficient to result in nicking activity, indicative of βPKC activation. The results indicate that peptide rVI, but not peptide I, is effective to stabilize PKC in an activated conformation that renders it susceptible to Arg-C under conditions of low PKC activators that would otherwise not render the enzyme susceptible to Arg-C.

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Example 10

Effects of RACK1 WD-40-derived Peptides on PKC

Autophosphorylation

Activated PKC is capable of autophosphorylation. Since 5 peptide rVI (SEQ ID NO:7) was effective to induce PKC translocation and GVBD in the absence of an activator such as insulin, the ability of the peptide to induce PKC autophosphorylation in the absence of PKC activators was assessed.

PKC autophosphorylation in the presence of 10 pseudosubstrate antibodies or the indicated peptides was carried out using a modification of the method described by Makowske, et al. Anti-pseudosubstrate antibodies, which were shown previously to induce autophosphorylation in the absence of PKC activators (Makowske, et al.) were used as a positive control. are shown in Figure 8. The results 15

Rat brain PKC (\sim 10 nM) was incubated with mild agitation in a final volume of 250 μl of overlay buffer, as in Example 1 either with anti-etaPKC pseudosubstrate antibodies (1:10 dilution, Life Technologies, Gaithersburg, MD) or with the indicated peptide (10 μ M). Where indicated, PS (50 μ g/ml), DG (0.8 μ g/ml) and CaCl $_2$ 20 (1 mM) were also added. The amount of autophosphorylation was determined after 2 hours for the reaction with the antipseudosubstrate antibodies, or after 15 minutes for the other samples. 50 μ l of a buffer comprised of 20 mM Tris-HCl (pH 7.5), 25 20 mM MgCl₂, 20 μ M ATP and 5 μ ci/ml [γ -³²P]ATP. The mixture was incubated for 15 minutes at room temperature and the reaction was stopped by adding 60 μl sample buffer (see Example 9). The samples were then boiled for 10 minutes, loaded onto a 10% SDS-PAGE mini gel and electrophoresed. The gel was fixed with 50% methanol and 10% acetic acid for 1 hour, and the autophosphorylation of PKC was 30 determined by autoradiography.

The results in Figure 8 show PKC autophosphorylation in the presence of DG, PS, and calcium (lane 1), in the presence of EGTA (lane 2), in the presence of anti-etaPKC pseudosubstrate antibodies (diluted 1:10 in 20 mM Tris-HCl; lane 3), in the 35 presence of peptide rVI (SEQ ID NO:7; 10 μM ; lane 4), in the presence of peptide I (SEQ ID NO:1; 10 μM ; lane 5), or in the presence of control peptide (SEQ ID NO:9; 10 μ M; lane 6).

Peptide rVI in the absence of PKC activators induced PKC autophosphorylation to over 80% of the autophosphorylation obtained in the presence of optimal concentration of PS, DG, and calcium (compare Fig. 8 lane 1 (control) with lane 4 (peptide rVI).

Neither peptide I nor control peptide induced PKC autophosphorylation in the absence of PKC activators (Fig. 8 lanes 5 and 6, respectively).

Example 11

Effects of RACK1 WD-40-derived Peptides on Histone

10 Phosphorylation by PKC

Incubation of PKC with peptide rVI (SEQ ID NO:7) induced histone phosphorylation by PKC. The method used was a modification of the protocol described by Mochly-Rosen, et al. (1987). The results are shown in Figure 9.

Histone type IIIs (Sigma Chemical Company, St. Louis, MO) was phosphorylated by PKC (~ 10 nM) in the absence (lane 1) and 15 presence of peptide rVI (10 μM) (lanes 2 and 3) and in the presence and absence of DG (0.8 μ g/ml), PS (50 μ g/ml) and CaCl₂ (1 mM) (lane 3). The results are expressed as percentage of control that is the amount of Histone phosphorylation by PKC in the presence of DG (0.8 μ g/ml), PS (50 μ g/ml) and CaCl₂ (1 mM). The results are 20 the average \pm SEM of two independent experiments. PKC was first incubated with the peptide rVI (10 μM) for 15 minutes in overlay buffer as described above. Histone type IIIs (40 $\mu \mathrm{g/ml}$) was added in Tris-HCl (20 mM), MgCl $_2$ (20 mM), ATP (20 μ M) and $[\gamma^{-32}P]$ ATP (5 μ ci/ml) with or without PS (50 μ g/ml), DG (0.8 μ g/ml) and CaCl₂ (1 25 mM). Histone phosphorylation was determined by autoradiography as

above.

PKC activators PS, DG, and calcium were not required for either peptide rVI-induced autophosphorylation or histone phosphorylation, suggesting that peptide rVI is an agonist of PKC activation.

In a related experiment, phosphorylation of histone type IIIs $(25\mu\text{M})$ by PKC (10~nM) was not inhibited by RACK1; rather, a 4.5 ± 0.1 fold increase of histone phosphorylation occurred when coincubated with ~100 nM RACK1 (n=2).

- 59 -

SEQUENCE LISTING

| 5 | (1) GENERAL INFORMATION: |
|----|--|
| | (i) APPLICANT: Mochly-Rosen, Daria |
| | Ron, Dorit |
| | Doily Doile |
| | (ii) TITLE OF INVENTION: WD-40 - Derived Peptides and Uses |
| 10 | Thereof |
| | • |
| | (iii) NUMBER OF SEQUENCES: 265 |
| | |
| 15 | (iv) CORRESPONDENCE ADDRESS: |
| | (A) ADDRESSEE: Dehlinger & Associates |
| | (B) STREET: P.O. Box 60850 |
| | (C) CITY: Palo Alto |
| | (D) STATE: CA |
| 20 | (E) COUNTRY: USA |
| | (F) ZIP: 94306-0850 |
| | (v) COMPUTER READABLE FORM: |
| | (A) MEDIUM TYPE: Floppy disk |
| | (B) COMPUTER: IBM PC compatible |
| 25 | (C) OPERATING SYSTEM: PC-DOS/MS-DOS |
| | (D) SOFTWARE: PatentIn Release #1.0, Version #1.25 |
| | |
| 30 | (vi) CURRENT APPLICATION DATA: |
| | (A) APPLICATION NUMBER: 08/190,802 |
| | (B) FILING DATE: 01-FEB-1994 |
| | (C) CLASSIFICATION: |
| 35 | (Viii) ATTORNEY/AGENT INFORMATION: |
| | (A) NAME: Fabian, Gary R. |
| | (B) REGISTRATION NUMBER: 33,875 |
| | (C) REFERENCE/DOCKET NUMBER: 8600-0139 |
| | |
| | (ix) TELECOMMUNICATION INFORMATION: |
| 40 | (A) TELEPHONE: (415) 324-0880 (B) TELEFAX: (415) 324-0880 |

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS: 45

(A) LENGTH: 15 amino acids

(B) TELEFAX: (415) 324-0960

```
(B) TYPE: amino acid(D) TOPOLOGY: unknown
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(ii) MOLECULE TYPE: peptide

5

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

10 (vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: Peptide I

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

15

Lys Gly Asp Tyr Glu Lys Ile Leu Val Ala Leu Cys Gly Gly Asn 15

(2) INFORMATION FOR SEQ ID NO:2:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 7 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

25

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 30 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: Peptide, rI, Fig. 1C

35

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

Val Thr Gln Ile Ala Thr Thr

- (2) INFORMATION FOR SEQ ID NO:3:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 7 amino acids
- 45 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

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(ii) MOLECULE TYPE: peptide
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- (iii) HYPOTHETICAL: NO
- 5 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: Peptide rII, Fig. 1C

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

Phe Val Ser Asp Val Val Ile 1 5

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- (2) INFORMATION FOR SEQ ID NO:4:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 7 amino acids

- (B) TYPE: amino acid(D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- 25 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 30 (C) INDIVIDUAL ISOLATE: Peptide rIII, Fig. 1C
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:
- Asp Val Leu Ser Val Ala Phe
 - (2) INFORMATION FOR SEQ ID NO:5:
- 40 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 7 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 45 (ii) MOLECULE TYPE: peptide

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(iii) HYPOTHETICAL: NO
        (iv) ANTI-SENSE: NO
        (vi) ORIGINAL SOURCE:
               (C) INDIVIDUAL ISOLATE: peptide rIV, Fig. 1C
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         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:
10
         Val Ser Cys Val Arg Phe Ser
          1
     (2) INFORMATION FOR SEQ ID NO:6:
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          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 7 amino acids
                (B) TYPE: amino acid
                (D) TOPOLOGY: unknown
20
          (ii) MOLECULE TYPE: peptide
         (iii) HYPOTHETICAL: NO
         (iv) ANTI-SENSE: NO
 25
          (vi) ORIGINAL SOURCE:
                 (C) INDIVIDUAL ISOLATE: Peptide rV, Fig. 1C
 30
           (xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:
           Gly Tyr Leu Asn Thr Val Thr
            1
  35
       (2) INFORMATION FOR SEQ ID NO:7:
            (i) SEQUENCE CHARACTERISTICS:
                  (A) LENGTH: 8 amino acids
                  (B) TYPE: amino acid
   40
                  (D) TOPOLOGY: unknown
            (ii) MOLECULE TYPE: peptide
      (iii) HYPOTHETICAL: NO
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(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: Peptide rVI, Fig. 1C

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

Asp Ile Ile Asn Ala Leu Cys Phe

10

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:

. 15

- (A) LENGTH: 7 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide

20

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 25 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: Peptide rVII, Fig. 1C
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

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30

Pro Gln Cys Thr Ser Leu Ala

(2) INFORMATION FOR SEQ ID NO:9:

35

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 6 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 45 (iv) ANTI-SENSE: NO

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: control peptide 1, homol. to RACK1 261-266, LKGKIL

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

Leu Lys Gly Lys Ile Leu

10

5

- (2) INFORMATION FOR SEQ ID NO:10:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 6 amino acids
- (B) TYPE: amino acid 15
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO 20
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- (C) INDIVIDUAL ISOLATE: control peptide 2, iden. to RACK1, 25 265 to 270 IIVDEL
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

30 Ile Ile Val Asp Glu Leu 1

(2) INFORMATION FOR SEQ ID NO:11:

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- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 18 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO 45

- 65 -(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: PKC substrate peptide, (Ser25) PKC(19-36) 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:11: Arg Phe Ala Arg Lys Gly Ser Leu Arg Gln Lys Asn Val His Glu Val 10 10 15 Lys Asn (2) INFORMATION FOR SEQ ID NO:12: 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 18 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 20 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 25 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: PKC Pseudosubstrate Inhibitor (PCK(19-36)) 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

Arg Phe Ala Arg Lys Gly Ala Leu Arg Gln Lys Asn Val His Glu Val 35 10 15

Lys Asn

- 40 (2) INFORMATION FOR SEQ ID NO:13:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 15 amino acids
 - (B) TYPE: amino acid
- 45 (D) TOPOLOGY: unknown

| - 66 - |
|--|
| (ii) MOLECULE TYPE: peptide |
| (iii) HYPOTHETICAL: NO |
| 5 (iv) ANTI-SENSE: NO |
| <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBH Peptide, rI, Fig. 24</pre> |
| 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:13: |
| Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro Asp Met Ile 10 15 |
| 15 (2) INFORMATION FOR SEQ ID NO:14: |
| (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 15 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| (ii) MOLECULE TYPE: peptide |
| (iii) HYPOTHETICAL: NO |
| 25 (iv) ANTI-SENSE: NO |
| (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBH Peptide rII, Fig. 24 |
| (xi) SEQUENCE DESCRIPTION: SEQ ID NO:14: |
| Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln Phe Ala Leu 15 1 10 15 |
| (2) INFORMATION FOR SEQ ID NO:15: |
| (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 15 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| (ii) MOLECULE TYPE: peptide |
| 45 (iii) HYPOTHETICAL: NO |

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: GBH Peptide rIII, Fig. 24

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

Asp Val Leu Ser Val Ala Phe Ser Ser Asp Asn Arg Gln Ile Val

10

- (2) INFORMATION FOR SEQ ID NO:16:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 15 amino acids

15 (B) TYPE: amino acid

(D) TOPOLOGY: unknown

- (ii) MOLECULE TYPE: peptide
- 20 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 25 (C) INDIVIDUAL ISOLATE: GBH Peptide rIV, Fig. 24
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:
- Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser Ser Asn Pro Ile

 1 5 10 15
 - (2) INFORMATION FOR SEQ ID NO:17:
- 35 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 15 amino acids

(B) TYPE: amino acid

- (D) TOPOLOGY: unknown
- 40 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

45

(vi) ORIGINAL SOURCE:

- WO 95/21252 - 68 -(C) INDIVIDUAL ISOLATE: GBH Peptide rV, Fig. 24 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:17: Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser Leu Cys Ala 10 5 (2) INFORMATION FOR SEQ ID NO:18: (i) SEQUENCE CHARACTERISTICS: 10 (A) LENGTH: 15 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 15 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 20 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBH Peptide rVI, Fig. 24 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:18: 25 Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys Phe Ser Pro 10 5 30 (2) INFORMATION FOR SEQ ID NO:19: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 1115 base pairs (B) TYPE: nucleic acid (C) STRANDEDNESS: double 35 (D) TOPOLOGY: linear (ii) MOLECULE TYPE: DNA (genomic) (iii) HYPOTHETICAL: NO 40 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 DNA Sequence, Fig. 1A 45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

GGCACGAGGG GTCGCGGTGG CAGCCGTGCG GTGCTTGGCT CCCTAAGCTA TCCGGTGCCA

5 TCCTTGTCGC TGCGGCGACT CGCAACATCT GCAGCCATGA CCGAGCAAAT GACCCTTCGT 120 GGGACCCTCA AGGGCCATAA TGGATGGGTT ACACAGATCG CCACCACTCC GCAGTTCCCG 180 GACATGATCC TGTCGGCGTC TCGAGACAAG ACCATCATCA TGTGGAAGCT GACCAGGGAT 10 240 GAGACCAACT ACGGCATACC ACAACGTGCT CTTCGAGGTC ACTCCCACTT TGTTAGCGAT 300 GTTGTCATCT CCTCTGATGG CCAGTTTGCC CTCTCAGGCT CCTGGGATGG AACCCTACGC 15 360 CTCTGGGATC TCACAACGGG CACTACCACG AGACGATTTG TCGGCCACAC CAAGGATGTG 420 CTGAGCGTGG CTTTCTCCTC TGACAACCGG CAGATTGTCT CTGGGTCCCG AGACAAGACC 480 ATTAAGTTAT GGAATACTCT GGGTGTCTGC AAGTACACTG TCCAGGATGA GAGTCATTCA 20 540 GAATGGGTGT CTTGTGTCCG CTTCTCCCCG AACAGCAGCA ACCCTATCAT CGTCTCCTGC 600 GGATGGGACA AGCTGGTCAA GGTGTGGAAT CTGGCTAACT GCAAGCTAAA GACCAACCAC 25 660 ATTGGCCACA CTGGCTATCT GAACACAGTG ACTGTCTCTC CAGATGGATC CCTCTGTGCT 720 TCTGGAGGCA AGGATGGCCA GGCTATGCTG TGGGATCTCA ATGAAGGCAA GCACCTTTAC 780 ACATTAGATG GTGGAGACAT CATCAATGCC TTGTGCTTCA GCCCCAACCG CTACTGGCTC 840 TGTGCTGCCA CTGGCCCCAG TATCAAGATC TGGGACTTGG AGGGCAAGAT CATGGTAGAT 900 GAACTGAAGC AAGAAGTTAT CAGCACCAGC AGCAAGGCAG AGCCACCCCA GTGTACCTCT 35 960 TTGGCTTGGT CTGCTGATGG CCAGACTCTG TTTGCTGGCT ATACCGACAA CTTGGTGCGT 1020 GTATGGCAGG TGACTATTGG TACCCGCTAA AAGTTTATGA CAGACTCTTA GAAATAAACT 1080 GGCTTTCTGA ААААААААА ААААААААА ААААА 1115

(2) INFORMATION FOR SEQ ID NO:20:

40

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 96 base pairs
 - (B) TYPE: nucleic acid

| (C) | STRANDEDNESS: | double |
|-----|---------------|--------|
|-----|---------------|--------|

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

5

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE: 10
 - (C) INDIVIDUAL ISOLATE: RACK1 rI DNA Sequence, Fig. 1A
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

GGCCATAATG GATGGGTTAC ACAGATCGCC ACCACTCCGC AGTTCCCGGA CATGATCCTG 15 60

TCGGCGTCTC GAGACAAGAC CATCATCATG TGGAAG

96 20

- (2) INFORMATION FOR SEQ ID NO:21:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 94 base pairs 25

(B) TYPE: nucleic acid

(C) STRANDEDNESS: double

(D) TOPOLOGY: linear

- (ii) MOLECULE TYPE: DNA (genomic) 30
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

35

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 rII DNA Sequence
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:21: 40

GGTCACTCCC ACTTGTTAG CGATGTTGTC ATCTCCTCTG ATGGCCAGTT TGCCCTCTCA 60

GGCTCCTGGG ATGGAACCCT ACGCCTCTGG GATC 45

- (2) INFORMATION FOR SEQ ID NO:22:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 93 base pairs
- (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: DNA (genomic)

5

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 15 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 rIII DNA Sequence, Fig. 1A
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

20

GGCCACACCA AGGATGTGCT GAGCGTGGCT TTCTCCTCTG ACAACCGGCA GATTGTCTCT

GGGTCCCGAG ACAAGACCAT TAAGTTATGG AAT

25 93

- (2) INFORMATION FOR SEQ ID NO:23:
 - (i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 99 base pairs

- (B) TYPE: nucleic acid
- (C) STRANDEDNESS: double
- (D) TOPOLOGY: linear
- 35 (ii) MOLECULE TYPE: DNA (genomic)
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 rIV DNA Sequence, Fig. 1A
- 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

AGTCATTCAG AATGGGTGTC TTGTGTCCGC TTCTCCCCGA ACAGCAGCAA CCCTATCATC 60

GTCTCCTGCG GATGGGACAA GCTGGTCAAG GTGTGGAAT

99 5

10

- (2) INFORMATION FOR SEQ ID NO:24:
 - (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 93 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: DNA (genomic) 15
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
- 20
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 rV DNA Sequence, Fig. 1A
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:24: 25

GGCCACACTG GCTATCTGAA CACAGTGACT GTCTCTCCAG ATGGATCCCT CTGTGCTTCT

- GGAGGCAAGG ATGGCCAGGC TATGCTGTGG GAT 30 93
 - (2) INFORMATION FOR SEQ ID NO:25:
- (i) SEQUENCE CHARACTERISTICS: 35
 - (A) LENGTH: 93 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear
- 40
- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO 45

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 rVI DNA Sequence, Fig. 1A
- 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

TTAGATGGTG GAGACATCAT CAATGCCTTG TGCTTCAGCC CCAACCGCTA CTGGCTCTGT

- 10 GCTGCCACTG GCCCCAGTAT CAAGATCTGG GAC 93
 - (2) INFORMATION FOR SEQ ID NO:26:
- 15 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 99 base pairs
 - (B) TYPE: nucleic acid
 - (C) STRANDEDNESS: double
 - (D) TOPOLOGY: linear

20

- (ii) MOLECULE TYPE: DNA (genomic)
- (iii) HYPOTHETICAL: NO
- 25 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 rVII DNA Sequence, Fig. 1A

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

AGCAAGGCAG AGCCACCCCA GTGTACCTCT TTGGCTTGGT CTGCTGATGG CCAGACTCTG

35

TTTGCTGGCT ATACCGACAA CTTGGTGCGT GTATGGCAG

(2) INFORMATION FOR SEQ ID NO:27:

40

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 317 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

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(ii) MOLECULE TYPE: protein

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| | (iii) HYPOTHETICAL: NO |
| | (iv) ANTI-SENSE: NO |
| 5 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RACK1 Amino Acid Sequence, Fig. 1C</pre> |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:27: |
| 10 | Met Thr Glu Gln Met Thr Leu Arg Gly Thr Leu Lys Gly His Asn Gly 1 10 15 |
| 15 | Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro Asp Met Ile Leu 25 30 |
| | Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys Leu Thr Arg Asp 45 |
| 20 | Glu Thr Asn Tyr Gly Ile Pro Gln Arg Ala Leu Arg Gly His Ser His 50 55 60 |
| | Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln Phe Ala Leu Ser 75 80 |
| 25 | Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp Leu Thr Thr Gly Thr 85 90 95 |
| 30 | Thr Thr Arg Arg Phe Val Gly His Thr Lys Asp Val Leu Ser Val Ala |
| | Phe Ser Ser Asp Asn Arg Gln Ile Val Ser Gly Ser Arg Asp Lys Thr 115 120 125 |
| 35 | Ile Lys Leu Trp Asn Thr Leu Gly Val Cys Lys Tyr Thr Val Gln Asp 130 135 140 |
| | Glu Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser 145 150 155 160 |
| 40 | Ser Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val 165 170 175 |
| 45 | Trp Asn Leu Ala Asn Cys Lys Leu Lys Thr Asn His Ile Gly His Thr 180 185 190 |

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| | - 75 - |
|----|--|
| | Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser Leu Cys Ala 195 200 205 |
| 5 | Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp Leu Asn Glu Gly 210 215 220 |
| | Lys His Leu Tyr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys 225 230 235 240 |
| 10 | Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile 245 250 255 |
| 15 | Lys Ile Trp Asp Leu Glu Gly Lys Ile Ile Val Asp Glu Leu Lys Gln 260 265 270 |
| | Glu Val Ile Ser Thr Ser Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser 275 280 285 |
| 20 | Leu Ala Trp Ser Ala Asp Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp 290 295 300 |
| | Asn Leu Val Arg Val Trp Gln Val Thr Ile Gly Thr Arg 305 310 315 |
| 25 | (2) INFORMATION FOR SEQ ID NO:28: |
| 30 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 501 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| 25 | (ii) MOLECULE TYPE: protein |
| 35 | (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO |
| 40 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Human 55 kDa protein (PWP homolog),</pre> |
| 45 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:28: |

Met Asn Arg Ser Arg Gln Val Thr Cys Val Ala Trp Val Arg Cys Gly

| | - 76 - |
|----|---|
| | 10 15 . |
| | Val Ala Lys Glu Thr Pro Asp Lys Val Glu Leu Ser Lys Glu Glu Val 20 25 30 |
| 5 | Lys Arg Leu Ile Ala Glu Ala Lys Glu Lys Leu Gln Glu Glu Gly Gly 35 40 45 |
| 10 | Gly Ser Asp Glu Glu Glu Thr Gly Ser Pro Ser Glu Asp Gly Met Gln 50 55 60 |
| | Ser Ala Arg Thr Gln Ala Arg Pro Arg Glu Pro Leu Glu Asp Gly Asp 70 75 80 |
| 15 | Pro Glu Asp Asp Arg Thr Leu Asp Asp Glu Leu Ala Glu Tyr Asp 90 95 |
| | Leu Asp Lys Tyr Asp Glu Glu Gly Asp Pro Asp Ala Glu Thr Leu Gly 100 105 110 |
| 20 | Glu Ser Leu Leu Gly Leu Thr Val Tyr Gly Ser Asn Asp Gln Asp Pro 115 120 125 |
| 25 | Tyr Val Thr Leu Lys Asp Thr Glu Gln Tyr Glu Arg Glu Asp Phe Leu 130 135 140 |
| | Ile Lys Pro Ser Asp Asn Leu Ile Val Cys Gly Arg Ala Glu Gln Asp 145 150 155 160 |
| 30 | Gln Cys Asn Leu Glu Val His Val Tyr Asn Gln Glu Glu Asp Ser Phe 165 170 175 |
| | Tyr Val His His Asp Ile Leu Leu Ser Ala Tyr Pro Leu Ser Val Glu 180 185 190 |
| 35 | Trp Leu Asn Phe Asp Pro Ser Pro Asp Asp Ser Thr Gly Asn Tyr Ile 195 200 205 |
| 40 | Ala Val Gly Asn Met Thr Pro Val Ile Glu Val Trp Asp Leu Asp Ile 210 215 220 |
| | Val Asp Ser Leu Glu Pro Val Phe Thr Leu Gly Ser Lys Leu Ser Lys 225 230 235 240 |
| 45 | Lys Lys Lys Lys Gly Lys Lys Ser Ser Ser Ala Glu Gly His Thi 245 250 255 |

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| | As | sp A | la V | al I 2 | eu A | .sp L | eu S | Ger 7 | | Asn 265 | Lys | Leu | Ile . | | Asn V 270 | al L | eu |
|------------|------------|------------|-------------|------------|-------------|-----------------|------------|-------------------|------|------------|------------|--------------|--------------|-------------|--------------|--------------|----|
| 5 | Al | a S | er A 2 | la S 75 | er A | la A | sp A | | hr ' | Val | Ile | Leu | | Asp M | Met S | er L | eu |
| | Gl | y Ly 29 | /s Pi 90 | ro A | la A | la Se | | eu A 95 | la V | /al : | His | | Asp I | ys V | al G | ln Th | ır |
| 10 | Le 30 | u Gl 5 | n Pł | ne H: | is Pı | o Pi 31 | ne G. | lu A | la G | ln : | | Leu : 315 | Ile S | er G | ly Se | er Ty | |
| 15 | Asj | p Ly | s Se | r Va | 11 A1 32 | a Le 5 | u Ty | /r As | sp C | | Arg : | Ser E | Pro A | sp G | lu Se 33 | er Hi 5 | s |
| | Arg | g Me | t Tr | p Ar 34 | g Ph O | e Se | r Gl | y Gl | | le G 45 | lu A | Arg V | al Ti | hr Ti 35 | | n His | 5 |
| 20 | Phe | e Se: | r Pro | о Су 5 | s Hi | s Ph | e Le | u Al 36 | | er T | hr A | sp A | sp G] | | ie Va | l Tyr | : |
| | Asn | Le: 370 | ı Ası | Ala | a Arg | g Sei | 37 | | s Pr | 0 I | le P | | hr L∈ 30 | u As | n Ala | a His | ; |
| 25 | Asn 385 | Asp | Glu | ı Ile | e Ser | Gl ₃ | / Lei | u As _l | p Le | u Se | | er G] 95 | ln Il | e Ly | s Gly | 7 Cys 400 | |
| 30 | Leu | Val | Thr | Ala | Ser 405 | Ala | Ası |) Lys | з Ту | r Va 41 | | ys Il | e Tr | p Ası | 9 Ile 415 | : Leu | |
| | Gly | Asp | Arg | Pro 420 | Ser | Leu | Val | . His | 42 | | g As | sp Me | t Ly: | 430 | : Gly | Val | |
| 35 | Leu | Phe | Cys 435 | Ser | Ser | Cys | Cys | Pro 440 | |) Le | u Pr | o Ph | e Ile 445 | | Ala | Phe | |
| | Gly | Gly 450 | Gln | Lys | Glu | Gly | Leu 455 | | Va] | Tr | p As | p Il. | | Thr | Val | Ser | |
| 40 | Ser 465 | Val | Asn | Glu | Ala | Phe 470 | Gly | Arg | Arg | r Gli | u Ar 47 | | ı Val | Leu | Gly | Ser 480 | |
| 1 5 | Ala | Arg | Asn | Ser | Ser 485 | Ile | Ser | Gly | Pro | Phe 490 | | y Sei | Arg | Ser | Ser 495 | Asp | |
| | Thr | Pro | Met | Glu | Ser | | | | | | | | | | | | |

500

| | (2) | INFORM | OITAN | N FOR | SEC |) ID | NO:2 | 29: | | | | | | | | | |
|----|-----|------------------|-------------|------------------------|-----------|-----------|---------------|-----------|------------|------------|-------------|-----------|-----------|-----------|-----------|-------------|-----------|
| 5 | | (i) [§] | (A) (B) | LENGT TYPE TOPOI | CH: 4 | 128 a | amino acid | o ac | ids | | | | | | | | |
| 10 | | (ii) | MOLE | CULE ' | TYPE | : pr | otei | n | | | | | | | | | |
| | | (iii) | нүро' | THETI | CAL: | NO | | | | | | | | | | | |
| 15 | | (iv) | ANTI | -sens | E: N | 0 | | | | | | | | | | | |
| | | (vi) | ORIG (C) | INAL INDI | SOUR | CE: | :SOL# | ATE: | AAC- | -RICI | H pro | otein | ı, Fi | .g. 1 | .2 | | |
| 20 | | (xi) | SEQU | TENCE | DESC | CRIP' | rion | : SE | Q ID | NO: | 29: | | | | | | |
| | | Pro 1 | Gly | Gly 1 | | Gln : | His : | Leu | Gln (| Gln (| Gln (10 | Gln (| Gln (| 3ln (| Gln (| Gln (15 | Gln |
| 25 | | Gln | Gln | Gln | Gln 20 | Gln | Gln | Gln | Gln | Gln 25 | Gln | Gln | Gln ' | Thr | Gln 30 | Val (| Gln |
| | | Glr | ı Leu | His | Asn | Gln | Leu | His | Gln 40 | Gln | His | Asn | Gln | Gln 45 | Ile | Gln | Gln |
| 30 | | Glı | n Ala | Gln | Ala | Thr | Gln | Gln 55 | His | Leu | Gln | Thr | Gln 60 | Gln | Tyr | Leu | Gln |
| 35 | | Se: | r Glī | ı Ile | His | Gln | Gln 70 | Ser | Gln | Gln | Ser | Gln 75 | Leu | Ser | Asn | Asn | Leu 80 |
| | | As | n Se | c Asn | Ser | Lys 85 | Glu | Ser | Thr | Asn | Ile 90 | Pro | Lys | Thr | Asn | Thr 95 | Gln |
| 40 | | ту | r Th | r Asn | Phe | | Ser | : Lys | : Asr | Lev 105 | ı Asp | Leu | Ala | Ser | Arg | Tyr | Phe |
| | | Se | er Gl | u Cys | | Thi | Lys | s Ası | Phe 120 | | e Gly | / Asr | Lys | 125 | Lys | Ser | Thr |

Ser Val Ala Trp Asn Ala Asn Gly Thr Lys Ile Ala Ser Ser Gly Ser

135

| | | | | | | | | | | | | | . • | | | |
|----|------------|--------------|---------------------|------------|--------------|------------|--------------|------------|--------------|------------|-------------|-----------------|------------|------------|------------|---------------|
| 5 | Asp 145 | | / Ile | e Val | l Arg | 7 Va: | |) As | n Ph | e As | p Pro 15 | | u Gl | y As | sn Se | er Asn 160 |
| | Asn | Asn | Asn | Asr | 165 | | n Asr | ı Th | r Se | r Se: | | ı Se | r Ly | s As | n As | n Asn 5 |
| 10 | Ile | Lys | Glu | Thr 180 | | : Glu | ı Leu | Ly: | 3 Gly 189 | | s Asp | Gl ₃ | y Se: | r Il 19 | | u Lys |
| | Ile | Ser | Trp 195 | Ser | Pro | Lys | Asn | Asr 200 | | Leu | ı Leu | Ala | 205 | | a Gl | y Thr |
| 15 | Asp | Lys 210 | Val | Ile | Lys | Ile | Trp 215 | Asp | Val | Lys | Ile | Gly 220 | | Cy: | s Ile | e Gly |
| 20 | Thr 225 | Val | Ser | Thr | Asn | Ser 230 | Glu | Asn | Ile | Asp | Val 235 | Arg | Trp | Ser | Pro | 240 |
| | Gly | Asp | His | Leu | Ala 245 | Leu | Ile | Asp | Leu | Pro 250 | Thr | Ile | Lys | Thr | Leu 255 | Lys |
| 25 | Ile | Tyr | Lys | Phe 260 | Asn | Gly | Glu | Glu | Leu 265 | Asn | Gln | Val | Gly | Trp 270 | | Asn |
| | Asn (| Gly | Asp 2 7 5 | Leu | Ile | Leu | Met | Ala 280 | Asn | Ser | Met | Gly | Asn 285 | Ile | Glu | Ala |
| 30 | Tyr 1 | Lys : 290 | Phe | Leu | Pro | Lys | Ser 295 | Thr | Thr | His | Val | Lys 300 | His | Leu | Lys | Thr |
| 35 | Leu 1 | Tyr (| Gly 1 | His | | Ala 310 | Ser | Ile | Tyr | Cys | Met 315 | Glu | Phe | Asp | Pro | Thr 320 |
| | Gly I | Lys : | Tyr 1 | Leu . | Ala . 325 | Ala | Gly | Ser | Ala | Asp 330 | Ser | Ile | Val | Ser | Leu 335 | Trp |
| 40 | Asp I | le (| Glu A | Asp | Met 1 | Met | Cys ' | Val | Lys 345 | Thr | Phe : | Ile | | Ser 350 | Thr | Phe |
| | Pro C | ys A | Arg S | Ger ' | Val : | Ser : | | Ser 360 | Phe . | Asp (| Gly (| | Phe 365 | Ile | Ala | Ala |
| 45 | Ser S | er F | he G | 3lu s | Ser : | | Ile (375 | Glu | Ile | Phe 1 | | Ile 380 | Glu | Ser | Ser | Gln |

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Pro Ile His Thr Ile Glu Cys Gly Val Ser Ser Leu Met Trp His Pro 395 390 385 Thr Leu Pro Leu Leu Ala Tyr Ala Pro Glu Ser Ile Asn Glu Asn Asn 410 405 5 Lys Asp Pro Ser Ile Arg Val Phe Gly Tyr His Ser 425 420 (2) INFORMATION FOR SEQ ID NO:30: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 517 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 15 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: BETA TRCP, Fig. 13 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:30: Met Glu Gly Phe Ser Cys Ser Leu Gln Pro Pro Thr Ala Ser Glu Arg 5 30 Glu Asp Cys Asn Arg Asp Glu Pro Pro Arg Lys Ile Ile Thr Glu Lys 30 25 20 Asn Thr Leu Arg Gln Thr Lys Leu Ala Asn Gly Thr Ser Ser Met Ile 35 40 35 Val Pro Lys Gln Arg Lys Leu Ser Ala Asn Tyr Glu Lys Glu Lys Glu 60 55 50 40 Leu Cys Val Lys Tyr Phe Glu Gln Trp Ser Glu Cys Asp Gln Val Glu 80 70 Phe Val Glu His Leu Ile Ser Arg Met Cys His Tyr Gln His Gly His

85

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| | Ile Asn Thr Tyr Leu Lys Pro Met Leu Gln Arg Asp Phe Ile Thr Ala 100 105 110 |
|----|--|
| 5 | Leu Pro Ala Arg Gly Leu Asp His Ile Ala Glu Asn Ile Leu Ser Tyr 115 120 125 |
| | Leu Asp Ala Lys Ser Leu Cys Ser Ala Glu Leu Val Cys Lys Glu Trp 130 135 140 |
| 10 | Tyr Arg Val Thr Ser Asp Gly Met Leu Trp Lys Lys Leu Ile Glu Arg 145 150 155 160 |
| 15 | Met Val Arg Thr Asp Ser Leu Trp Arg Gly Leu Ala Glu Arg Arg Gly 165 170 175 |
| | Trp Gly Gln Tyr Leu Phe Lys Asn Lys Pro Pro Asp Gly Lys Thr Pro 180 185 190 |
| 20 | Pro Asn Ser Phe Tyr Arg Ala Leu Tyr Pro Lys Ile Ile Gln Asp Ile 195 200 205 Glu Thr Ile Glu Ser Arg T |
| 25 | Glu Thr Ile Glu Ser Asn Trp Arg Cys Gly Arg His Ser Leu Gln Arg 210 215 220 Ile His Cys Arg Ser Clu The Cys |
| | Ile His Cys Arg Ser Glu Thr Ser Lys Gly Val Tyr Cys Leu Gln Tyr 225 230 235 240 Asp Asp Glr Lys Ile Val Ser The |
| 30 | Asp Asp Gln Lys Ile Val Ser Gly Leu Arg Asp Asn Thr Ile Lys Ile 245 250 255 |
| | Trp Asp Lys Asn Thr Leu Glu Cys Lys Arg Val Leu Met Gly His Thr 260 265 270 Gly Ser Val Leu Cys Leu Glo Typ Asy Gl |
| 35 | Gly Ser Val Leu Cys Leu Gln Tyr Asp Glu Arg Val Ile Ile Thr Gly 275 280 285 Ser Asp Ser Thr Val Arg Val Trp Asp Val Asn Thr Gly Glu Met Leu |
| 40 | 295 300 |
| | Asn Thr Leu Ile His His Cys Glu Ala Val Leu His Leu Arg Phe Asn 305 310 315 320 Asn Gly Met Met Val Thr Cys Ser Lev 2 |
| 45 | Asn Gly Met Met Val Thr Cys Ser Lys Asp Arg Ser Ile Ala Val Trp 325 330 335 Asp Met Ala Ser Ala Thr Assa Tile |
| | Asp Met Ala Ser Ala Thr Asp Ile Thr Leu Arg Arg Val Leu Val Gly |

- 82 -His Arg Ala Ala Val Asn Val Val Asp Phe Asp Asp Lys Tyr Ile Val Ser Ala Ser Gly Asp Arg Thr Ile Lys Val Trp Asn Thr Ser Thr Cys Glu Phe Val Arg Thr Leu Asn Gly His Lys Arg Gly Ile Ala Cys Leu Gln Tyr Arg Asp Arg Leu Val Val Ser Gly Ser Ser Asp Asn Thr Ile Arg Leu Trp Asp Ile Glu Cys Gly Ala Cys Leu Arg Val Leu Glu Gly His Glu Glu Leu Val Arg Cys Ile Arg Phe Asp Asn Lys Arg Ile Val Ser Gly Ala Tyr Asp Gly Lys Ile Lys Val Trp Asp Leu Val Ala Ala Leu Asp Pro Arg Ala Pro Ala Gly Thr Leu Cys Leu Arg Thr Leu Val Glu His Ser Gly Arg Val Phe Arg Leu Gln Phe Asp Glu Phe Gln Ile Val Ser Ser Ser His Asp Asp Thr Ile Leu Ile Trp Asp Phe Leu Asn Asp Pro Gly Leu Ala (2) INFORMATION FOR SEQ ID NO:31: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 906 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: NO

| | | | | | | | - 8 | 3 - | | | | | | | | |
|----|------------|------------|----------------|-------------|-----------|-------------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | (iv | r) A1 | VTI-S | ENSE | : NC |) | | | | | | | | | | |
| 5 | (vi | | RIGIN (C) I | | | | COLAT | E: b | eta- | prim | ie-cc | p, F | ig. | 14 | | |
| | (xi |) SE | QUEN | CE D | ESCR | IPTI | ON: | SEQ | ID N | 0:31 | : | | | | | |
| 10 | Me: 1 | t Pr | o Le | u Ar | g Le | u As | p Il | e Ly | s Ar | g Ly 10 | s Le | u Th | r Al | a Ar | g Se 15 | r Asp |
| | Arg | y Vai | l Ly: | s Se: 20 | r Val | l As _] | p Le | u Hi: | 5 Pro | o Th: | r Gli | u Pro | o Tr | р Ме 30 | t Le | u Ala |
| 15 | Ser | . Let | и Туг 35 | : Ası | ı Gly | / Sei | r Val | l Cys | s Val | l Trp | Ası | n His | 5 Gl 45 | ı Thi | r Glı | n Thr |
| 20 | Leu | Va] | l Lys | Thr | Phe | Glu | Val | . Cys | Asp |) Leu | Pro | Val | . Arg | , Ala | a Ala | Lys |
| | Phe 65 | · Val | . Ala | Arg | Lys | Asn 70 | Trp | Val | Val | Thr | Gly | Ala | Asp | Asp | Met | Gln 80 |
| 25 | Ile | Arg | Val | Phe | Asn 85 | Tyr | Asn | Thr | Leu | Glu 90 | Arg | Val | His | Met | Phe 95 | Glu |
| | Ala | His | Ser | Asp 100 | Tyr | Ile | Arg | Cys | Ile 105 | Ala | Val | His | Pro | Thr 110 | Gln | Pro |
| 30 | Phe | Ile | Leu 115 | Thr | Ser | Ser | Asp | Asp 120 | Met | Leu | Ile | Lys | Leu 125 | Trp | Asp | Trp |
| 35 | Asp | Lys 130 | Lys | Trp | Ser | Cys | Ser 135 | Gln | Val | Phe | Glu | Gly 140 | His | Thr | His | Tyr |
| | Val 145 | Met | Gln | Ile | | Ile 150 | Asn | Pro | Lys | Asp | Asn 155 | Asn | Gln | Phe | Ala | Ser 160 |
| 40 | Ala | Ser | Leu | Asp | Arg | Thr | Ile | Lys | Val | Trp | Gln | Leu | Gly | Ser | Ser | Ser |

Tyr Tyr Ser Gly Gly Asp Lys Pro Tyr Leu Ile Ser Gly Ala Asp Asp

Pro Asn Phe Thr Leu Glu Gly His Glu Lys Gly Val Asn Cys Ile Asp

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|----|--|
| | Arg Leu Val Lys Ile Trp Asp Tyr Gln Asn Lys Thr Cys Val Gln Thr 210 215 220 |
| 5 | Leu Glu Gly His Ala Gln Asn Val Ser Cys Ala Ser Phe His Pro Glu 235 230 235 240 |
| | Leu Pro Ile Ile Ile Thr Gly Ser Glu Asp Gly Thr Val Arg Ile Trp 245 250 255 |
| 10 | His Ser Ser Thr Tyr Arg Leu Glu Ser Thr Leu Asn Tyr Gly Met Glu 260 265 270 |
| | Arg Val Trp Cys Val Ala Ser Leu Arg Gly Ser Asn Asn Val Ala Leu 275 280 285 |
| 15 | Gly Tyr Asp Glu Gly Ser Ile Ile Val Lys Leu Gly Arg Glu Glu Pro 290 295 300 |
| 20 | Ala Met Ser Met Asp Ala Asn Gly Lys Ile Ile Trp Ala Lys His Ser 305 310 315 320 |
| | Glu Val Gln Gln Ala Asn Leu Lys Ala Met Gly Asp Ala Glu Ile Lys 325 330 335 |
| 25 | Asp Gly Glu Arg Leu Pro Leu Ala Val Lys Asp Met Gly Ser Cys Glu 340 345 350 |
| | Ile Tyr Pro Gln Thr Ile Gln His Asn Pro Asn Gly Arg Phe Val Val 355 360 365 |
| 30 | Val Cys Gly Asp Gly Glu Tyr Ile Ile Tyr Thr Ala Met Ala Leu Arg 370 375 380 |
| 35 | Asn Lys Ser Phe Gly Ser Ala Gln Glu Phe Ala Trp Ala His Asp Ser 385 390 395 400 |
| | Ser Glu Tyr Ala Ile Arg Glu Ser Asn Ser Val Val Lys Ile Phe Lys 405 410 415 |
| 40 | Asn Phe Lys Glu Lys Lys Ser Phe Lys Pro Asp Phe Gly Ala Glu Ser 420 425 430 |
| | Ile Tyr Gly Gly Phe Leu Leu Gly Val Arg Ser Val Asn Gly Leu Ala 435 440 445 |
| 45 | Phe Tyr Asp Trp Glu Asn Thr Glu Leu Ile Arg Arg Ile Glu Ile Gln |

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| | | 43 | U | | | | 45 | 5 | | | | 46 | 0 | | | | |
|----|------------|------------|--------------|--------------|--------------|------------|------------|------------|-------------|------------|------------|------------|------------|-------------|------------|------|-----------|
| 5 | Pro 465 | Lys | s His | s Il | e Phe | e Trj | | r As | p Se | er Gl | у Gl 47 | | u Va | ı cy | rs I | | Ala 80 |
| | Thr | Glu | ı Glu | se: | r Phe 485 | | e Ile | e Le | u Ly | s Ty | | u Se | r Gl | u Ly | s Va | | eu |
| 10 | Ala | Ala | Gln | 500 | Thr | His | s Glu | ı Gl | y Va. 50 | | r Glu | ı Asp | Gl; | y Il | | u A | sp |
| | Gly | Phe | Glu 515 | Val | . Leu | Gly | Glu | 11e | | n Glu | ı Ile | · Va] | Lys | | r Gl | y L | eu |
| 15 | Trp | Val 530 | Gly | Asp | Cys | Phe | Ile 535 | | Thi | s Ser | Ser | Val 540 | | Ar <u>c</u> | J Le | u As | ≅n |
| 20 | Tyr 545 | Tyr | Val | Gly | Gly | Glu 550 | Ile | Val | Thr | : Ile | Ala 555 | His | Leu | Asp | Arg | 7 Th | |
| | Met | Tyr | Leu | Leu | Gly 565 | Tyr | Ile | Pro | Lys | Asp 570 | Asn | Arg | Leu | Tyr | Le: | | У |
| 25 | Asp | Lys | Glu | Leu 580 | Asn | Ile | Val | Ser | Tyr 585 | | Leu | Leu | Val | Ser 590 | Val | Le | u |
| | Glu ' | Tyr | Gln 595 | Thr | Ala | Val | Met | Arg 600 | Arg | Asp | Phe | Ser | Met 605 | Ala | Asp | Ly | s |
| 30 | Val 1 | Leu 610 | Pro | Thr | Ile | Pro | Lys 615 | Glu | Gln | Arg | | Arg 620 | Val | Ala | His | Ph€ | € |
| 35 | Leu 6 | 3lu | Lys | Gln | | Phe 630 | Lys | Gln | Gln | Ala | Leu 635 | Thr | Val | Ser | Thr | Asp | |
| | Pro G | Slu 1 | His i | | Phe (| Glu | Leu . | Ala | Leu | Gln 650 | Leu | Gly | Glu | | Lys 655 | Ile | ! |
| 40 | Ala T | ;Àx (| Gln 1 | Leu . 560 | Ala V | Val (| Glu i | | Glu 665 | Ser | Glu (| Gln . | | Trp 670 | Lys | Gln | ı |
| | Leu A | la (| 3lu I 675 | Leu . | Ala : | Ile : | | Lys 680 | Cys | Pro | Phe (| | Leu 685 | Ala | Gln | Glu | |
| 45 | Cys L | eu F 90 | His H | lis i | Ala (| | Asp : | Tyr | Gly | Gly : | | Leu : | Leu | Leu . | Ala | Thr | |

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| | - 86 - | |
|----|--|------------|
| | Ala Ser Gly Asn Ala Ser Met Val Asn Lys Leu Ala Glu Gly Ala Gl 705 710 715 72 | Lu, 20 |
| 5 | Arg Asp Gly Lys Asn Asn Val Ala Phe Met Ser Tyr Phe Leu Gln Gl 725 730 735 | ly |
| | Lys Leu Asp Ala Cys Leu Glu Leu Leu Ile Arg Thr Gly Arg Leu P 740 745 750 | ro |
| 10 | Glu Ala Ala Phe Leu Ala Arg Thr Tyr Leu Pro Ser Gln Val Ser A 755 760 765 | rg |
| | Val Val Lys Leu Trp Arg Glu Asn Leu Ser Lys Val Asn Gln Lys A 770 780 | la. |
| 15 | Ala Glu Ser Leu Ala Asp Pro Thr Glu Tyr Glu Asn Leu Phe Pro G 785 790 795 8 | 1y 100 |
| 20 | Leu Lys Glu Ala Phe Val Val Glu Glu Trp Val Lys Glu Thr His A | Ala |
| | Asp Leu Trp Pro Ala Lys Gln Tyr Pro Leu Val Thr Pro Asn Glu C 820 825 830 | 3lu |
| 25 | Arg Asn Val Met Glu Glu Ala Lys Gly Phe Gln Pro Ser Arg Ser 1845 | Ala |
| | Ala Gln Gln Glu Leu Asp Gly Lys Pro Ala Ser Pro Thr Pro Val 850 855 860 | Ile |
| 30 | Val Thr Ser Gln Thr Ala Asn Lys Glu Glu Lys Ser Leu Leu Glu 865 870 875 | Leu 880 |
| 35 | Glu Val Asp Leu Asp Asn Leu Glu Ile Glu Asp Ile Asp Thr Thr 885 890 895 | Asp |
| | Ile Asn Leu Asp Glu Asp Ile Leu Asp Asp 900 905 | |
| | A INFORMATION FOR SEO ID NO:32: | |

40 (2) INFORMATION FOR SEQ ID NO:32:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 779 amino acids
 - (B) TYPE: amino acid
- 45 (D) TOPOLOGY: unknown

| | (11) MOLECULE TYPE: protein | | | | | | | | | | | | | | | |
|----|-----------------------------|------------|-------------|------------|-------------------|------------|------------|------------|-------------|------------|------------|------------|------------|-------------|------------|------------|
| | (iii | .) ну | POTE | ETIC | 'AL: | NO | | | | | | | | | | |
| 5 | (iv | ') AN | TI-S | ENSE | : NO | | | | | | | | | | | |
| | (vi | | | | OURC: | | OLAT: | E: C | DC4 | / CD | C20 | prot | ein, | Fig | . 15 | |
| 10 | | | | | | | | | | | | | | | | • |
| | (xi |) SE | QUEN | CE D | ESCR: | IPTI(| : NC | SEQ : | ID N | 0:32 | : | | | | | |
| 15 | Mei 1 | t Gl | y Se: | r Phe | e Pro | Let | ı Ala | a Gla | ı Phe | Pro |) Le | ı Ar | g Asj | p Il | e Pr | o Val |
| | Pro | ту: | r Sei | 7yı 20 | Arg | y Val | . Ser | Gly | / Gly 25 | / Ile | ≥ Ala | a Sei | s Sei | r Gly 30 | / Se: | r Val |
| 20 | Thr | Ala | a Leu 35 | ı Val | . Thr | Ala | Ala | Gly 40 | Thr | His | Arg | Asr | Ser 45 | : Ser | Thi | Ala |
| | Lys | Thr 50 | Val | Glu | Thr | Glu | Asp 55 | Gly | Glu | Glu | . Asp | Ile 60 | Asp | Glu | Tyr | Gln |
| 25 | Arg 65 | Lys | Arg | Ala | Ala | Gly 70 | Ser | Gly | Glu | Ser | Thr 75 | Pro | Glu | Arg | Ser | Asp 80 |
| 30 | Phe | Lys | Arg | Val | Lys 85 | His | Asp | Asn | His | Lys 90 | Thr | Leu | His | Pro | Val 95 | Asn |
| | Leu | Gln | Asn | Thr 100 | Gly | Ala | Ala | Ser | Val 105 | Asp | Asn | Asp | Gly | Leu 110 | His | Asn |
| 35 | Leu | Thr | Asp 115 | Ile | Ser | Asn | Asp | Ala 120 | Glu | Lys | Leu | Leu | Met 125 | Ser | Val | Asp |
| | Asp | Gly 130 | Ser | Ala | Ala | Pro | Ser 135 | Thr | Leu | Ser | Val | Asn 140 | Met | Gly | Val | Ala |
| 40 | Ser 145 | His | Asn | Val | Ala | Ala 150 | Pro | Thr | Thr | Val | Asn 155 | Ala | Ala | Thr | Ile | Thr 160 |
| 45 | Gly | Ser | Asp | Val | Ser 165 | Asn | Asn | Val | Asn | Ser 170 | Ala | Thr | Ile | Asn | Asn 175 | Pro |
| | Met | Glu | Glu | Gly | Ala | Leu | Pro | Leu | Ser | Pro | Thr | Ala | Ser | Ser | Pro | Gly |

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| | | _ | 00 | | 100 |
|----|--------------------|----------------------|----------------------------|---------------------------|------------------------|
| | | 180 | 18 | 35 | 190 |
| | Thr Thr Thr | | Lys Thr Th | nr Lys Thr Ile Asn 205 | Asn Asn Asn |
| 5 | Asn Ile Ala | Asp Leu Ile | e Glu Ser Ly 215 | ys Asp Ser Ile Ile 220 | Ser Pro Glu |
| 10 | Tyr Leu Ser 225 | Asp Glu Ile | | la Ile Asn Asn Asn 235 | Leu Pro His 240 |
| | Ala Tyr Phe | e Lys Asn Leu 245 | u Leu Phe A | rg Leu Val Ala Asr 250 | 1 Met Asp Arg 255 |
| 15 | Ser Glu Le | ı Ser Asp Let 260 | u Gly Thr L 2 | eu Ile Lys Asp Ası 865 | n Leu Lys Arg 270 |
| | Asp Leu Ile 27 | | u Pro Phe G 280 | Slu Ile Ser Leu Lys 28 | s Ile Phe Asn 5 |
| 20 | Tyr Leu Gl | n Phe Glu As | sp Ile Ile <i>I</i> 295 | Asn Ser Leu Gly Va 300 | l Ser Gln Asn |
| 25 | 305 | 31 | 10 | Thr Ser Leu Trp Ly 315 | 320 |
| | | 325 | | Lys Gly Phe Asn Se 330 | 335 |
| 30 | Lys Leu Se | er Gln Lys Ty 340 | | Leu Ser Gln Gln As 345 | p Arg Leu Arg 350 |
| 25 | 3! | 55 | 360 | | 55 |
| 35 | 370 | | 375 | Leu Arg Gly His Me 380 | |
| 40 | 385 | 3 | 390 | Asn Tyr Val Ile T 395 | 400 |
| | | 405 | | Ser Ile Asn Lys L 410 | 415 |
| 45 | Gln Leu S | Ger Gly His A | Asp Gly Gly | Val Trp Ala Leu I 425 | Lys Tyr Ala His 430 |

| | Gly Gly Ile Leu Val Ser Gly Ser Thr Asp Arg Thr Val Arg Val Trp 435 440 445 |
|----|---|
| 5 | Asp Ile Lys Lys Gly Cys Cys Thr His Val Phe Glu Gly His Asn Ser 450 455 460 |
| | Thr Val Arg Cys Leu Asp Ile Val Glu Tyr Lys Asn Ile Lys Tyr Ile 465 470 475 480 |
| 10 | Val Thr Gly Ser Arg Asp Asn Thr Leu His Val Trp Lys Leu Pro Lys 485 490 495 |
| 15 | Glu Ser Ser Val Pro Asp His Gly Glu Glu His Asp Tyr Pro Leu Val 500 505 510 |
| | Phe His Thr Pro Glu Glu Asn Pro Tyr Phe Val Gly Val Leu Arg Gly 515 520 525 |
| 20 | His Met Ala Ser Val Arg Thr Val Ser Gly His Gly Asn Ile Val Val 530 535 540 |
| | Ser Gly Ser Tyr Asp Asn Thr Leu Ile Val Trp Asp Val Ala Gln Met 545 550 560 |
| 25 | Lys Cys Leu Tyr Ile Leu Ser Gly His Thr Asp Arg Ile Tyr Ser Thr 565 570 575 |
| 30 | Ile Tyr Asp His Glu Arg Lys Arg Cys Ile Ser Ala Ser Met Asp Thr 580 585 590 |
| | Thr Ile Arg Ile Trp Asp Leu Glu Asn Ile Trp Asn Asn Gly Glu Cys 595 600 605 |
| 35 | Ser Tyr Ala Thr Asn Ser Ala Ser Pro Cys Ala Lys Ile Leu Gly Ala 610 615 620 |
| | Met Tyr Thr Leu Gln Gly His Thr Ala Leu Val Gly Leu Leu Arg Leu 625 630 635 640 |
| 40 | Ser Asp Lys Phe Leu Val Ser Ala Ala Ala Asp Gly Ser Ile Arg Gly 645 650 655 |
| 45 | Trp Asp Ala Asn Asp Tyr Ser Arg Lys Phe Ser Tyr His His Thr Asn 660 665 670 |
| | Leu Ser Ala Ile Thr Thr Phe Tyr Val Ser Asp Asn Ile Leu Val Ser |

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- 90 -680 685 675 Gly Ser Glu Asn Gln Phe Asn Ile Tyr Asn Leu Arg Ser Gly Lys Leu 700 695 690 5 Val His Ala Asn Ile Leu Lys Asp Ala Asp Gln Ile Trp Ser Val Asn 715 710 Phe Lys Gly Lys Thr Leu Val Ala Ala Val Glu Lys Asp Gly Gln Ser 735 730 725 10 Phe Leu Glu Ile Leu Asp Phe Ser Lys Ala Ser Lys Ile Asn Tyr Val 745 740 Ser Asn Pro Val Asn Ser Ser Ser Ser Ser Leu Glu Ser Ile Ser Thr 15. 765 760 755 Ser Leu Gly Leu Thr Arg Thr Thr Ile Ile Pro 775 770 20 (2) INFORMATION FOR SEQ ID NO:33: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 318 amino acids (B) TYPE: amino acid 25 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO 30-(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBLP -CHLAMIDOMONAS HOMOLOG, Fig. 16 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:33: Met Ala Glu Thr Leu Thr Leu Arg Ala Thr Leu Lys Gly His Thr Asn 40 10 5 Trp Val Thr Ala Ile Ala Thr Pro Leu Asp Pro Ser Ser Asn Thr Leu 25

Leu Ser Ala Ser Arg Asp Lys Ser Val Leu Val Trp Glu Leu Glu Arg

20

Ser Glu Ser Asn Tyr Gly Tyr Ala Arg Lys Ala Leu Arg Gly His Ser His Phe Val Gln Asp Val Val Ile Ser Ser Asp Gly Gln Phe Cys Leu Thr Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp Leu Asn Thr Gly Thr Thr Thr Arg Arg Phe Val Gly His Thr Lys Asp Val Leu Ser Val Ala Phe Ser Val Asp Asn Arg Gln Ile Val Ser Gly Ser Arg Asp Lys Thr Ile Lys Leu Trp Asn Thr Leu Gly Glu Cys Lys Tyr Thr Ile Gly Glu Pro Glu Gly His Thr Glu Trp Val Ser Cys Val Arg Phe Ser Pro Met Thr Thr Asn Pro Ile Ile Val Ser Gly Gly Trp Asp Lys Met Val Lys Val Trp Asn Leu Thr Asn Cys Lys Leu Lys Asn Asn Leu Val Gly His His Gly Tyr Val Asn Thr Val Thr Val Ser Pro Asp Gly Ser Leu

Cys Ala Ser Gly Gly Lys Asp Gly Ile Ala Met Leu Trp Asp Leu Ala 210 215 220

Glu Gly Lys Arg Leu Tyr Ser Leu Asp Ala Gly Asp Val Ile His Cys
235 230 235 240

Leu Cys Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gln Ser

245 250 255

Ser Ile Lys Ile Trp Asp Leu Glu Ser Lys Ser Ile Val Asp Asp Leu 260 265 270

Arg Pro Glu Phe Asn Ile Thr Ser Lys Lys Ala Gln Val Pro Tyr Cys
275
280
285

105

100

45

- 92 -Val Ser Leu Ala Trp Ser Ala Asp Gly Ser Thr Leu Tyr Ser Gly Tyr 300 295 290 Thr Asp Gly Gln Ile Arg Val Trp Ala Val Gly His Ser Leu 310 5 305 (2) INFORMATION FOR SEQ ID NO:34: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 658 amino acids 10 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 15 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 20 (C) INDIVIDUAL ISOLATE: cop-1 protein, Fig. 17 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:34: 25 Met Glu Glu Ile Ser Thr Asp Pro Val Val Pro Ala Val Lys Pro Asp 15 10 5 1 Pro Arg Thr Ser Ser Val Gly Glu Gly Ala Asn Arg His Glu Asn Asp 25 20 30 Asp Gly Gly Ser Gly Ser Glu Ile Gly Ala Pro Asp Leu Asp Lys 45 40 35 Asp Leu Leu Cys Pro Ile Cys Met Gln Ile Ile Lys Asp Ala Phe Leu 35 55 Thr Ala Cys Gly His Ser Phe Cys Tyr Met Cys Ile Ile Thr His Leu 75 70 40 Arg Asn Lys Ser Asp Cys Pro Cys Cys Ser Gln His Leu Thr Asn Asn 95 90 85 Gln Leu Tyr Pro Asn Phe Leu Leu Asp Lys Leu Leu Lys Lys Thr Ser

| | Ala Arg His Val Ser Lys Thr Ala Ser Pro Leu Asp Gln Phe Arg Glu 115 120 125 |
|----|--|
| 5 | Ala Leu Gln Arg Gly Cys Asp Val Ser Ile Lys Glu Val Asp Asn Leu 130 135 140 |
| | Leu Thr Leu Leu Ala Glu Arg Lys Arg Lys Met Glu Gln Glu Glu Ala 145 150 155 160 |
| 10 | Glu Arg Asn Met Gln Ile Leu Leu Asp Phe Leu His Cys Leu Arg Lys 165 170 175 |
| 15 | Gln Lys Val Asp Glu Leu Asn Glu Val Gln Thr Asp Leu Gln Tyr Ile 180 185 190 |
| | Lys Glu Asp Ile Asn Ala Val Glu Arg His Arg Ile Asp Leu Tyr Arg 195 200 205 |
| 20 | Ala Arg Asp Arg Tyr Ser Val Lys Leu Arg Met Leu Gly Asp Asp Pro 210 215 220 Ser Thr Arg Asp Ala Tyr De Title 1 |
| 25 | Ser Thr Arg Asn Ala Trp Pro His Glu Lys Asn Gln Ile Gly Phe Asn 225 230 235 240 Ser Asn Ser Leu Ser Ile Arg Gly |
| | Ser Asn Ser Leu Ser Ile Arg Gly Gly Asn Phe Val Gly Asn Tyr Gln 245 250 255 Asn Lys Lys Val Glu Gly Lys Ala Gln Gly Ser Ser His Gly Leu Pro |
| 30 | 260 265 270 Lys Lys Asp Ala Leu Ser Gly Ser Asp Ser Gln Ser Leu Asn Gln Ser |
| | 275 280 285 Thr Val Ser Met Ala Arg Lys Lys Arg Ile His Ala Gln Phe Asn Asp |
| 35 | Leu Gln Glu Cys Tyr Leu Gln Lys Arg Gln Leu Ala Asp Gln Pro |
| 40 | Asn Ser Lys Gln Glu Asn Asp Lys Ser Val Val Arg Arg Glu Gly Tyr |
| | Ser Asn Gly Leu Ala Asp Phe Gln Ser Val Leu Thr Thr Phe Thr Arg |
| 45 | Tyr Ser Arg Leu Arg Val Ile Ala Glu Ile Arg His Gly Asp Ile Phe |

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| | - 94 - |
|----|---|
| | 355 360 365 |
| | His Ser Ala Asn Ile Val Ser Ser Ile Glu Phe Asp Arg Asp Asp Glu 370 380 |
| 5 | Leu Phe Ala Thr Ala Gly Val Ser Arg Cys Ile Lys Val Phe Asp Phe 385 390 395 400 |
| 10 | Ser Ser Val Val Asn Glu Pro Ala Asp Met Gln Cys Pro Ile Val Glu 405 410 415 |
| | Met Ser Thr Arg Ser Lys Leu Ser Cys Leu Ser Trp Asn Lys His Glu 420 425 430 |
| 15 | Lys Asn His Ile Ala Ser Ser Asp Tyr Glu Gly Ile Val Thr Val Trp 435 440 445 |
| | Asp Val Thr Thr Arg Gln Ser Leu Met Glu Thr Glu Glu Asn Glu Lys 450 455 460 |
| 20 | Arg Ala Trp Ser Val Asp Phe Ser Arg Thr Glu Pro Ser Met Leu Val 465 470 475 480 |
| 25 | Ser Gly Ser Asp Asp Cys Lys Val Lys Val Trp Cys Thr Arg Gln Glu 485 490 495 |
| | Ala Ser Val Ile Asn Ile Asp Met Lys Ala Asn Ile Cys Cys Val Lys 500 505 510 |
| 30 | Tyr Asn Pro Gly Ser Ser Asn Tyr Ile Ala Val Gly Ser Ala Asp His 515 520 525 |
| · | His Ile His Tyr Tyr Asp Leu Arg Asn Ile Ser Gln Pro Leu His Val 530 535 540 |
| 35 | Phe Ser Gly His Lys Lys Ala Val Ser Tyr Met Lys Phe Leu Ser Asn 545 550 555 560 |
| 40 | Asn Glu Leu Ala Ser Ala Ser Thr Asp Ser Thr Leu Arg Leu Trp Asp 565 570 575 |
| | Val Lys Asp Asn Leu Pro Val Arg Thr Phe Arg Gly His Thr Asn Glu 580 585 590 |
| 45 | Lys Asn Phe Val Gly Leu Thr Val Asn Ser Glu Tyr Leu Ala Cys Gly 595 600 605 |

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Ser Glu Thr Thr Arg Tyr Val Tyr His Lys Glu Ile Thr Arg Pro Val
610 615 620

Thr Ser His Arg Phe Gly Ser Pro Asp Met Asp Asp Ala Glu Lys Arg 625 630 635 640

Gln Val Pro Thr Leu Leu Val Arg Phe Ala Gly Arg Val Ile Val Pro
645 650 655

10 Arg Cys

(2) INFORMATION FOR SEQ ID NO:35:

- 15 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 440 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 20 (ii) MOLECULE TYPE: protein
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

25

40

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: CORO PROTEIN, Fig. 18
- 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

Met Ser Lys Val Val Arg Ser Ser Lys Tyr Arg His Val Phe Ala Ala 1 5 10 15

35 Gln Pro Lys Lys Glu Glu Cys Tyr Gln Asn Leu Lys Thr Lys Ser Ala 20 25 30

Val Trp Asp Ser Asn Tyr Val Ala Ala Asn Thr Arg Tyr Ile Trp Asp
35 40 45

Ala Ala Gly Gly Ser Phe Ala Val Glu Ala Ile Pro His Ser Gly
50 55 60

Lys Thr Thr Ser Val Pro Leu Phe Asn Gly His Lys Ser Ala Val Leu
45 65 70 75 80

- 96 **-**

| | - 96 - |
|-----|--|
| | Asp Ile Ala Phe His Pro Phe Asn Glu Asn Leu Val Gly Ser Val Ser 85 90 95 |
| 5 | Glu Asp Cys Asn Ile Cys Ile Trp Gly Ile Pro Glu Gly Gly Leu Thr 100 105 110 |
| | Asp Ser Ile Ser Thr Pro Leu Gln Thr Leu Ser Gly His Lys Arg Lys 115 120 125 |
| 10 | Val Gly Thr Ile Ser Phe Gly Pro Val Ala Asp Asn Val Ala Val Thr 130 135 140 |
| | Ser Ser Gly Asp Phe Leu Val Lys Thr Trp Asp Val Glu Gln Gly Lys 145 150 155 160 |
| 15, | Asn Leu Thr Thr Val Glu Gly His Ser Asp Met Ile Thr Ser Cys Glu 165 170 175 |
| 20 | His Asn Gly Ser Gln Ile Val Thr Thr Cys Lys Asp Lys Lys Ala Arg 180 185 190 |
| | Val Phe Asp Pro Arg Thr Asn Ser Ile Val Asn Glu Val Val Cys His 195 200 205 |
| 25 | Gln Gly Val Lys Asn Ser Arg Ala Ile Phe Ala Lys Asp Lys Val Ile 210 215 220 |
| | Thr Val Gly Phe Ser Lys Thr Ser Glu Arg Glu Leu His Ile Tyr Asp 225 230 235 240 |
| 30 | Pro Arg Ala Phe Thr Thr Pro Leu Ser Ala Gln Val Val Asp Ser Ala 245 250 255 |
| 35 | Ser Gly Leu Leu Met Pro Phe Tyr Asp Ala Asp Asn Ser Ile Leu Tyr 260 265 270 |
| | Leu Ala Gly Lys Gly Asp Gly Asn Ile Arg Tyr Tyr Glu Leu Val Asp 275 280 285 |
| 40 | Glu Ser Pro Tyr Ile His Phe Leu Ser Glu Phe Lys Ser Ala Thr Pro 290 295 300 |
| | Gln Arg Gly Leu Cys Phe Leu Pro Lys Arg Cys Leu Asn Thr Ser Glu 305 310 315 320 |
| 45 | Cys Glu Ile Ala Arg Gly Leu Lys Val Thr Pro Phe Thr Val Glu Pro |

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325 330 335 Ile Ser Phe Arg Val Pro Arg Lys Ser Asp Ile Phe Gln Gly Asp Ile 340 345 5 Tyr Pro Asp Thr Tyr Ala Gly Glu Pro Ser Leu Thr Ala Glu Gln Trp 355 360 Val Ser Gly Thr Asn Ala Glu Pro Lys Thr Val Ser Leu Ala Gly Gly 10 Phe Val Lys Lys Ala Ser Ala Val Glu Phe Lys Pro Val Val Gln Val 385 390 395 400 Gln Glu Gly Pro Lys Asn Glu Lys Glu Leu Arg Glu Glu Tyr Glu Lys 15 405 410 Leu Lys Ile Arg Val Ala Tyr Leu Glu Ser Glu Ile Val Lys Lys Asp 420 425 430 20 Ala Lys Ile Lys Glu Leu Thr Asn 435 440 (2) INFORMATION FOR SEQ ID NO:36: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 445 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO 35 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Coronin (p55), Fig. 19 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:36: Met Ser Lys Val Val Arg Ser Ser Lys Tyr Arg His Val Phe Ala Ala 5 10 15 45

Gln Pro Lys Lys Glu Glu Cys Tyr Gln Asn Leu Lys Val Thr Lys Ser

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Ala Trp Asp Ser Asn Tyr Val Ala Ala Asn Thr Arg Tyr Phe Gly Val Ile Trp Asp Ala Ala Gly Gly Gly Ser Phe Ala Val Ile Pro His Glu Ala Ser Gly Lys Thr Thr Ser Val Pro Leu Phe Asn Gly His Lys Ser Ala Val Leu Asp Ile Ala Phe His Pro Phe Asn Glu Asn Leu Val Gly Ser Val Ser Glu Asp Cys Asn Ile Cys Ile Trp Gly Ile Pro Glu Gly Gly Leu Thr Asp Ser Ile Ser Thr Pro Leu Gln Thr Leu Ser Gly His Lys Arg Lys Val Gly Thr Ile Ser Phe Gly Pro Val Ala Asp Asn Val Ala Val Thr Ser Ser Gly Asp Phe Leu Val Lys Thr Trp Asp Val Glu Gln Gly Lys Asn Leu Thr Thr Val Glu Gly His Ser Asp Met Ile Thr Ser Cys Glu Trp Asn His Asn Gly Ser Gln Ile Val Thr Thr Cys Lys Asp Lys Lys Ala Arg Val Phe Asp Pro Arg Thr Asn Ser Ile Val Asn Glu Val Val Cys His Gln Gly Val Lys Asn Ser Arg Ala Ile Phe Ala Lys Asp Lys Val Ile Thr Val Gly Phe Ser Lys Thr Ser Glu Arg Glu Leu His Ile Tyr Asp Pro Arg Ala Phe Thr Thr Pro Leu Ser Ala Gln Val Val Asp Ser Ala Ser Gly Leu Leu Met Pro Phe Tyr Asp Ala Asp

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| | Asn Ser Ile Leu Tyr Leu Ala Gly Lys Gly Asp Gly Asn Ile Arg Tyr 275 280 285 |
|----|--|
| 5 | Tyr Glu Leu Val Asp Glu Ser Pro Tyr Ile His Phe Leu Ser Glu Phe 290 295 300 |
| | Lys Ser Ala Thr Pro Gln Arg Gly Leu Cys Phe Leu Pro Lys Arg Cys 305 310 315 320 |
| 10 | Leu Asn Thr Ser Glu Cys Glu Ile Ala Arg Gly Leu Lys Val Thr Pro 325 330 335 |
| 15 | Phe Thr Val Glu Pro Ile Ser Phe Arg Val Pro Arg Lys Ser Asp Ile 340 345 350 |
| | Phe Gln Gly Asp Ile Tyr Pro Asp Thr Tyr Ala Gly Glu Pro Ser Leu 355 360 365 |
| 20 | Thr Ala Glu Gln Trp Val Ser Gly Thr Asn Ala Glu Pro Lys Thr Val |
| | Ser Leu Ala Gly Gly Phe Val Lys Lys Ala Ser Ala Val Glu Phe Lys 385 390 395 400 |
| 25 | Pro Val Val Gln Val Gln Glu Gly Pro Lys Asn Glu Lys Glu Leu Arg 405 410 415 |
| 30 | Glu Glu Tyr Glu Lys Leu Lys Ile Arg Val Ala Tyr Leu Glu Ser Glu 420 425 430 |
| | Ile Val Lys Lys Asp Ala Lys Ile Lys Glu Leu Thr Asn 435 440 445 |
| 35 | (2) INFORMATION FOR SEQ ID NO:37: |
| | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 431 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |

- (ii) MOLECULE TYPE: protein
- (iii) HYPOTHETICAL: NO
- 45 (iv) ANTI-SENSE: NO

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(vi) ORIGINAL SOURCE:

- (C) INDIVIDUAL ISOLATE: CSTF 50kDa, Fig. 20
- 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

Met Tyr Arg Thr Lys Val Gly Leu Lys Asp Arg Gln Gln Leu Tyr Lys

1 10 15

Leu Ile Ile Ser Gln Leu Leu Tyr Asp Gly Tyr Ile Ser Ile Ala Asn 20 25 30

> Gly Leu Ile Asn Glu Ile Lys Pro Gln Ser Val Cys Ala Pro Ser Glu 35 40 45

- Gln Leu Leu His Leu Ile Lys Leu Gly Met Glu Asn Asp Asp Thr Ala
 50 55 60
- Val Gln Tyr Ala Ile Gly Arg Ser Asp Thr Val Ala Pro Gly Thr Gly
 20 65 70 75 80
 - Ile Asp Leu Glu Phe Asp Ala Asp Val Gln Thr Met Ser Pro Glu Ala 85 90 95
- 25 Ser Glu Tyr Glu Thr Cys Tyr Val Thr Ser His Lys Gly Pro Cys Arg 100 105 110
 - Val Ala Thr Tyr Ser Arg Asp Gly Gln Leu Ile Ala Thr Gly Ser Ala 115 120 125

Asp Ala Ser Ile Lys Ile Leu Asp Thr Glu Arg Met Leu Ala Lys Ser 130 135 140

- Ala Met Pro Ile Glu Val Met Met Asn Glu Thr Ala Gln Gln Asn Met

 150 155 160
 - Glu Asn His Pro Val Ile Arg Thr Leu Tyr Asp His Val Asp Glu Val
 165 170 175
- 40 Thr Cys Leu Ala Phe His Pro Thr Glu Gln Ile Leu Ala Ser Gly Ser 180 185 190
 - Arg Asp Tyr Thr Leu Lys Leu Phe Asp Tyr Ser Lys Pro Ser Ala Lys
 195 200 205
- 45 Arg Ala Phe Lys Tyr Ile Gln Glu Ala Glu Met Leu Arg Ser Ile Ser

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210 215 220

Phe His Pro Ser Gly Asp Phe Ile Leu Val Gly Thr Gln His Pro Thr Leu Arg Leu Tyr Asp Ile Asn Thr Phe Gln Cys Phe Val Ser Cys Asn Pro Gln Asp Gln His Thr Asp Ala Ile Cys Ser Val Asn Tyr Asn Ser Ser Ala Asn Met Tyr Val Thr Gly Ser Lys Asp Gly Cys Ile Lys Leu Trp Asp Gly Val Ser Asn Arg Cys Ile Thr Thr Phe Glu Lys Ala His Asp Gly Ala Glu Val Cys Ser Ala Ile Phe Ser Lys Asn Ser Lys Tyr Ile Leu Ser Ser Gly Lys Asp Ser Val Ala Lys Leu Trp Glu Ile Ser Thr Gly Arg Thr Leu Val Arg Tyr Thr Gly Ala Gly Leu Ser Gly Arg Gln Val His Arg Thr Gln Ala Val Phe Asn His Thr Glu Asp Tyr Val Leu Leu Pro Asp Glu Arg Thr Ile Ser Leu Cys Cys Trp Asp Ser Arg Thr Ala Glu Arg Arg Asn Leu Leu Ser Leu Gly His Asn Asn Ile Val Arg Cys Ile Val His Ser Pro Thr Asn Pro Gly Phe Met Thr Cys Ser Asp Asp Phe Arg Ala Arg Phe Trp Tyr Arg Arg Ser Thr Thr Asp

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 340 amino acids

(B) TYPE: amino acid

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| | (D) TOPOLOGY: unknown | |
|----|--|---|
| | (ii) MOLECULE TYPE: protein | |
| 5 | (iii) HYPOTHETICAL: NO | |
| | (iv) ANTI-SENSE: NO | |
| 10 | (vi) ORIGINAL SOURCE:(C) INDIVIDUAL ISOLATE: G-Beta 1 bovine, Fig. 21 | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:38: | |
| 15 | Met Ser Glu Leu Asp Gln Leu Arg Gln Glu Ala Glu Gln Leu Lys Asn 1 5 10 15 | |
| | Gln Ile Arg Asp Ala Arg Lys Ala Cys Ala Asp Ala Thr Leu Ser Gln 20 25 30 | |
| 20 | Ile Thr Asn Asn Ile Asp Pro Val Gly Arg Ile Gln Met Arg Thr Arg 35 40 45 | |
| 25 | Arg Thr Leu Arg Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Gly 50 55 60 | |
| | Thr Asp Ser Arg Leu Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile 65 70 75 80 | |
| 30 | Ile Trp Asp Ser Tyr Thr Thr Asn Lys Val His Ala Ile Pro Leu Arg 85 90 95 | |
| | Ser Ser Trp Val Met Thr Cys Ala Tyr Ala Pro Ser Gly Asn Tyr Val | |
| 35 | Ala Cys Gly Gly Leu Asp Asn Ile Cys Ser Ile Tyr Asn Leu Lys Thr 115 120 125 | |
| 40 | Arg Glu Gly Asn Val Arg Val Ser Arg Glu Leu Ala Gly His Thr Gly 130 135 140 | , |
| | Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Gln Ile Val Thr Ser 145 150 155 160 | : |
| 45 | Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp Ile Glu Thr Gly Gln Gl: | n |

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Thr Thr Thr Phe Thr Gly His Thr Gly Asp Val Met Ser Leu Ser Leu 180 185 190 Ala Pro Asp Thr Arg Leu Phe Val Ser Gly Ala Cys Asp Ala Ser Ala 5 195 200 205 Lys Leu Trp Asp Val Arg Glu Gly Met Cys Arg Gln Thr Phe Thr Gly 210 215 His Glu Ser Asp Ile Asn Ala Ile Cys Phe Phe Pro Asn Gly Asn Ala 10 225 230 235 240 Phe Ala Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp Leu Arg 245 250 15 Ala Asp Gln Glu Leu Met Thr Tyr Ser His Asp Asn Ile Ile Cys Gly 260 265 Ile Thr Ser Val Ser Phe Ser Lys Ser Gly Arg Leu Leu Leu Ala Gly 20 275 280 Tyr Asp Asp Phe Asn Cys Asn Val Trp Asp Ala Leu Lys Ala Asp Arg 290 295 Ala Gly Val Leu Ala Gly His Asp Asn Arg Val Ser Cys Leu Gly Val 25 305 315 320 Thr Asp Asp Gly Met Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu 330 335 30 Lys Ile Trp Asn (2) INFORMATION FOR SEQ ID NO:39: 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 326 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown

(iii) HYPOTHETICAL: NO

(ii) MOLECULE TYPE: protein

45 (iv) ANTI-SENSE: NO

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| | - 104 - |
|------|---|
| | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta- bovine (2), Fig. 22</pre> |
| 5 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:39: |
| | Arg Asn Gln Ile Arg Asp Ala Arg Lys Ala Cys Gly Asp Ser Thr Leu 1 10 15 |
| 10 | Thr Gln Ile Thr Ala Gly Leu Asp Pro Val Gly Arg Ile Gln Met Arg 20 25 30 |
| | Thr Arg Arg Thr Leu Arg Gly His Leu Ala Lys Ile Tyr Ala Met His 35 40 45 |
| 15 . | Trp Gly Thr Asp Ser Arg Leu Leu Val Ser Ala Ser Gln Asp Gly Lys 50 55 60 |
| 20 | Leu Ile Ile Trp Asp Ser Glu Gly Asn Val Arg Tyr Thr Thr Asn Lys 65 70 75 80 |
| | Val His Ala Ile Pro Leu Arg Ser Ser Trp Val Met Thr Cys Ala Tyr 85 90 95 |
| 25 | Ala Pro Ser Gly Asn Phe Val Ala Cys Gly Gly Leu Asp Asn Ile Cys 100 105 110 |
| | Ser Ile Tyr Ser Leu Lys Thr Arg Val Ser Arg Glu Leu Pro Gly His 115 120 125 |
| 30 | Thr Gly Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Gln Ile Ile 130 135 140 |
| 35 | Thr Ser Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp Ile Glu Thr Gly 145 150 155 160 |
| | Gln Gln Thr Val Gly Phe Ala Gly His Ser Gly Asp Val Met Ser Leu 165 170 175 |
| 40 | Ser Leu Ala Pro Asp Gly Arg Thr Phe Val Ser Gly Ala Cys Asp Ala 180 185 190 |
| | Ser Ile Lys Leu Trp Asp Val Arg Asp Ser Met Cys Arg Gln Thr Phe 195 200 205 |

Ile Gly His Glu Ser Asp Ile Asn Ala Val Ala Phe Phe Pro Asn Gly

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210 215 220

Tyr Ala Phe Thr Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp
225 230 235 240

Leu Arg Ala Asp Gln Glu Leu Leu Met Tyr Ser His Asp Asn Ile Ile
245 250 255

Cys Gly Ile Thr Ser Val Ala Phe Ser Arg Ser Gly Arg Leu Leu 260 265 270

Ala Gly Tyr Asp Asp Phe Asn Cys Asn Ile Trp Asp Ala Met Lys Gly
275 280 285

Asp Arg Ala Gly Val Leu Ala Gly His Asp Asn Arg Val Ser Cys Leu
290 295 300

Gly Val Thr Asp Asp Gly Met Ala Val Ala Thr Gly Ser Trp Asp Ser 305 310 315 320

Phe Leu Lys Ile Trp Asn 325

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 340 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

- (iii) HYPOTHETICAL: NO
- 35 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: G- BETA DROSOPH, Fig. 23

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

Met Asn Glu Leu Asp Ser Leu Arg Gln Glu Ala Glu Ser Leu Lys Asn 1 5 10 15

Ala Ile Arg Asp Ala Arg Lys Ala Ala Cys Asp Thr Ser Leu Leu Gln

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Ala Ala Thr Ser Leu Glu Pro Ile Gly Arg Ile Gln Met Arg Thr Arg Arg Thr Leu Arg Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Gly Asn Asp Ser Arg Asn Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile Val Trp Asp Ser His Thr Thr Asn Lys Val His Ala Ile Pro Leu Arg Ser Ser Trp Val Met Thr Cys Ala Tyr Ala Pro Ser Gly Ser Tyr Val Ala Cys Gly Gly Leu Asp Asn Met Cys Ser Ile Tyr Asn Leu Lys Thr Arg Glu Gly Asn Val Arg Val Ser Arg Glu Leu Pro Gly His Gly Gly Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Gln Ile Val Thr Ser Ser Gly Asp Met Ser Cys Gly Leu Trp Asp Ile Glu Thr Gly Leu Gln Val Thr Ser Phe Leu Gly His Thr Gly Asp Val Met Ala Leu Ser Leu 30 -Ala Pro Gln Cys Lys Thr Phe Val Ser Gly Ala Cys Asp Ala Ser Ala Lys Leu Trp Asp Ile Arg Glu Gly Val Cys Lys Gln Thr Phe Pro Gly His Glu Ser Asp Ile Asn Ala Val Thr Phe Phe Pro Asn Gly Gln Ala Phe Ala Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp Ile Arg Ala Asp Gln Glu Leu Ala Met Tyr Ser His Asp Asn Ile Ile Cys Gly

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- 107 -Ile Thr Ser Val Ala Phe Ser Lys Ser Gly Arg Leu Leu Leu Ala Gly 275 280 285 Tyr Asp Asp Phe Asn Cys Asn Val Trp Asp Thr Met Lys Ala Glu Arg 5 295 Ser Gly Ile Leu Ala Gly His Asp Asn Arg Val Ser Cys Leu Gly Val 305 310 Thr Glu Asn Gly Met Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu 10 325 330 Arg Val Trp Asn 340 15 (2) INFORMATION FOR SEQ ID NO:41: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 317 amino acids 20 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 25 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 30 (C) INDIVIDUAL ISOLATE: G-BETA HUMAN, Fig. 24 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:41: 35 Met Thr Glu Gln Met Thr Leu Arg Gly Thr Leu Lys Gly His Asn Gly 1 5 Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro Asp Met Ile Leu 20 40

Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys Leu Thr Arg Asp 35 40 45

Glu Thr Asn Tyr Gly Ile Pro Gln Arg Ala Leu Arg Gly His Ser His

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| | - 108 - |
|----|--|
| | Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln Phe Ala Leu Ser 70 75 80 |
| 5 | Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp Leu Thr Thr Gly Thr 85 90 95 |
| | Thr Thr Arg Arg Phe Val Gly His Thr Lys Asp Val Leu Ser Val Ala 100 105 110 |
| 10 | Phe Ser Ser Asp Asn Arg Gln Ile Val Ser Gly Ser Arg Asp Lys Thr 115 120 125 |
| | Ile Lys Leu Trp Asn Thr Leu Gly Val Cys Lys Tyr Thr Val Gln Asp 130 135 140 |
| 15 | Glu Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser 145 150 155 160 |
| 20 | Ser Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val 165 170 175 |
| | Trp Asn Leu Ala Asn Cys Lys Leu Lys Thr Asn His Ile Gly His Thr 180 185 190 |
| 25 | Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser Leu Cys Ala 195 200 205 |
| | Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp Leu Asn Glu Gly 210 215 220 |
| 30 | Lys His Leu Tyr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys 225 230 235 240 |
| 35 | Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile 245 250 255 |
| | Lys Ile Trp Asp Leu Glu Gly Lys Ile Ile Val Asp Glu Leu Lys Gln 260 265 270 |
| 40 | Glu Val Ile Ser Thr Ser Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser 275 280 285 |
| | Leu Ala Trp Ser Ala Asp Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp 290 295 300 |
| 45 | Asn Leu Val Arg Val Trp Gln Val Thr Ile Gly Thr Arg |

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(2) INFORMATION FOR SEQ ID NO:42:

- 5 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 340 amino acids
 - (B) TYPE: amino acid(D) TOPOLOGY: unknown
- 10 (ii) MOLECULE TYPE: protein
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
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- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: G-Beta 2 (Human), Fig. 25
- 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:
 - Met Ser Glu Leu Glu Gln Leu Arg Gln Glu Ala Glu Gln Leu Arg Asn

 1 10 15
- 25 Gln Ile Arg Asp Ala Arg Lys Ala Cys Gly Asp Ser Thr Leu Thr Gln
 20 25 30
- Ile Thr Ala Gly Leu Asp Pro Val Gly Arg Ile Gln Met Arg Thr Arg
 35 40 45
 - Arg Thr Leu Arg Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Gly
 50 55 60
- Thr Asp Ser Arg Leu Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile
 35 65 70 75 80
 - Ile Trp Asp Ser Tyr Thr Thr Asn Lys Val His Ala Ile Pro Leu Arg
- Ser Ser Trp Val Met Thr Cys Ala Tyr Ala Pro Ser Gly Asn Phe Val
 - Ala Cys Gly Gly Leu Asp Asn Ile Cys Ser Ile Tyr Ser Leu Lys Thr 115 120 125
- Arg Glu Gly Asn Val Arg Val Ser Arg Glu Leu Pro Gly His Thr Gly

- 110 -Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Gln Ile Ile Thr Ser Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp Ile Glu Thr Gly Gln Gln Thr Val Gly Phe Ala Gly His Ser Gly Asp Val Met Ser Leu Ser Leu Ala Pro Asp Gly Arg Thr Phe Val Ser Gly Ala Cys Asp Ala Ser Ile Lys Leu Trp Asp Val Arg Asp Ser Met Cys Arg Gln Thr Phe Ile Gly His Glu Ser Asp Ile Asn Ala Val Ala Phe Phe Pro Asn Gly Tyr Ala Phe Thr Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp Leu Arg Ala Asp Gln Glu Leu Leu Met Tyr Ser His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ala Phe Ser Arg Ser Gly Arg Leu Leu Ala Gly Tyr Asp Asp Phe Asn Cys Asn Ile Trp Asp Ala Met Lys Gly Asp Arg Ala Gly Val Leu Ala Gly His Asp Asn Arg Val Ser Cys Leu Gly Val

Thr Asp Asp Gly Met Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu
325 330 335

Lys Ile Trp Asn

(2) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 29 amino acids

(B) TYPE: amino acid

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- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: protein
- 5 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 10 (C) INDIVIDUAL ISOLATE: G-Beta 4 (mouse), Fig. 26
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:
- Lys Lys Asx Glu Thr Asx Val Asn Met Gly Arg Tyr Thr Pro Arg Ile

 1 5 10 15

Lys His Ile Lys Arg Pro Arg Arg Thr Asp Xaa Xaa Gly
20 25

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- (2) INFORMATION FOR SEQ ID NO:44:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 718 amino acids
- 25 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: protein
- 30 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 35 (C) INDIVIDUAL ISOLATE: GROUCHO PROTEIN DROSOPH, Fig. 27
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:
- Met Tyr Pro Ser Pro Val Arg His Pro Ala Ala Gly Gly Pro Pro Pro 1 5 10 15
 - Gln Gly Pro Ile Lys Phe Thr Ile Ala Asp Thr Leu Glu Arg Ile Lys
 20 25 30
- Glu Glu Phe Asn Phe Leu Gln Ala His Tyr His Ser Ile Lys Leu Glu

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|----|--|
| | 35 40 45 |
| | Cys Glu Lys Leu Ser Asn Glu Lys Thr Glu Met Gln Arg His Tyr Val 50 55 60 |
| 5 | Met Tyr Tyr Glu Met Ser Tyr Gly Leu Asn Val Glu Met His Lys Gln 65 70 75 80 |
| 10 | Thr Glu Ile Ala Lys Arg Leu Asn Thr Leu Ile Asn Gln Leu Leu Pro 85 90 95 |
| u | Phe Leu Gln Ala Asp His Gln Gln Gln Val Leu Gln Ala Val Glu Arg 100 105 110 |
| 15 | Ala Lys Gln Val Thr Met Gln Glu Leu Asn Leu Ile Ile Gly Gln Gln 115 120 125 |
| | Ile His Ala Gln Gln Val Pro Gly Gly Pro Pro Gln Pro Met Gly Ala 130 135 140 |
| 20 | Leu Asn Pro Phe Gly Ala Leu Gly Ala Thr Met Gly Leu Pro His Gly 145 150 155 160 |
| 25 | Pro Gln Gly Leu Leu Asn Lys Pro Pro Glu His His Arg Pro Asp Ile 165 170 175 |
| | Lys Pro Thr Gly Leu Glu Gly Pro Ala Ala Glu Glu Arg Leu Arg 180 185 190 |
| 30 | Asn Ser Val Ser Pro Ala Asp Arg Glu Lys Tyr Arg Thr Arg Ser Pro 195 200 205 |
| | Leu Asp Ile Glu Asn Asp Ser Lys Arg Arg Lys Asp Glu Lys Leu Gln 210 215 220 |
| 35 | Glu Asp Glu Gly Glu Lys Ser Asp Gln Asp Leu Val Val Asp Val Ala 225 230 235 240 |
| 40 | Asn Glu Met Glu Ser His Ser Pro Arg Pro Asn Gly Glu His Val Ser 245 250 255 |
| | Met Glu Val Arg Asp Arg Glu Ser Leu Asn Gly Glu Arg Leu Glu Lys 260 265 270 |
| 45 | Pro Ser Ser Ser Gly Ile Lys Gln Glu Arg Pro Pro Ser Arg Ser Gly 275 280 285 |

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| | Ser Ser Ser Ser Arg Ser Thr Pro Ser Leu Lys Thr Lys Asp Met Glu 290 295 300 |
|----|--|
| 5 | Lys Pro Gly Thr Pro Gly Ala Lys Ala Arg Thr Pro Thr Pro Asn Ala 305 310 315 320 |
| | Ala Ala Pro Ala Pro Gly Val Asn Pro Lys Gln Met Met Pro Gln Gly 325 330 335 |
| 10 | Pro Pro Pro Ala Gly Tyr Pro Gly Ala Pro Tyr Gln Arg Pro Ala Asp 340 345 350 |
| 15 | Pro Tyr Gln Arg Pro Pro Ser Asp Pro Ala Tyr Gly Arg Pro Pro Pro 355 360 365 |
| | Met Pro Tyr Asp Pro His Ala His Val Arg Thr Asn Gly Ile Pro His 370 375 380 |
| 20 | Pro Ser Ala Leu Thr Gly Gly Lys Pro Ala Tyr Ser Phe His Met Asn 385 390 395 400 |
| | Gly Glu Gly Ser Leu Gln Pro Val Pro Phe Pro Pro Asp Ala Leu Val 405 410 415 |
| 25 | Gly Val Gly Ile Pro Arg His Ala Arg Gln Ile Asn Thr Leu Ser His 420 425 430 |
| 30 | Gly Glu Val Val Cys Ala Val Thr Ile Ser Asn Pro Thr Lys Tyr Val 445 |
| | Tyr Thr Gly Gly Lys Gly Cys Val Lys Val Trp Asp Ile Ser Gln Pro 450 455 460 |
| 35 | Gly Asn Lys Asn Pro Val Ser Gln Leu Asp Cys Leu Gln Arg Asp Asn 465 470 475 480 |
| | Tyr Ile Arg Ser Val Lys Leu Leu Pro Asp Gly Arg Thr Leu Ile Val 485 490 495 |
| 40 | Gly Gly Glu Ala Ser Asn Leu Ser Ile Trp Asp Leu Ala Ser Pro Thr 500 505 510 |
| 45 | Pro Arg Ile Lys Ala Glu Leu Thr Ser Ala Ala Pro Ala Cys Tyr Ala 515 520 525 |
| | Leu Ala Ser Pro Asp Ser Lys Val Cys Phe Ser Cys Cys Ser Asp Gly |

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Asn Ile Ala Val Trp Asp Leu His Asn Glu Ile Leu Val Arg Gln Phe Gln Gly His Thr Asp Gly Ala Ser Cys Ile Asp Ile Ser Pro Asp Gly Ser Arg Leu Trp Thr Gly Gly Leu Asp Asn Thr Val Arg Ser Trp Asp Leu Arg Glu Gly Arg Gln Leu Gln Gln His Asp Phe Ser Ser Gln Ile Phe Ser Leu Gly Tyr Cys Pro Thr Gly Asp Trp Leu Ala Val Gly Met Glu Asn Ser His Val Glu Val Leu His Ala Ser Lys Pro Asp Lys Tyr Gln Leu His Leu His Glu Ser Cys Val Leu Ser Leu Arg Phe Ala Ala Cys Gly Lys Trp Phe Val Ser Thr Gly Lys Asp Asn Leu Leu Asn Ala Trp Arg Thr Pro Tyr Gly Ala Ser Ile Phe Gln Ser Lys Glu Thr Ser Ser Val Leu Ser Cys Asp Ile Ser Thr Asp Asp Lys Tyr Ile Val Thr Gly Ser Gly Asp Lys Lys Ala Thr Val Tyr Glu Val Ile Tyr

(2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 341 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: NO

28

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| | (17 | r) A1 | NTI-S | ENSI | E: NC |) | | | | • | | | | | | |
|----|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|-------------|------------|------------|------------|
| 5 | (vi | | RIGIN | | | | OLAT | E: G | TP b | oindi | .ng p | rote | ein | (squ: | id), | Fig. |
| - | (xi |) SE | QUEN | CE E | ESCR | IPTI | ON: | SEQ | ID N | iO : 45 | : | | | | | |
| 10 | Me 1 | t Th | r Se | r Gl | u Le 5 | u Gl | u Ala | a Le | u Ar | g Gl 10 | n Gl | u Th | r Gl | u Gl | n Le | u Lys |
| | Ası | n Gl | n Il | e Ar 20 | g Gl | u Ala | a Arg | J Ly: | s Al. 25 | a Ala | a Ala | a As | p Th | r Th 30 | | u Ala |
| 15 | Met | t Ala | a Thi | r Ala | a Ası | ı Val | l Glu | 40 | o Vai | l Gly | y Arg | g Ile | ≘ Gl: 45 | n Me | t Ar | g Thr |
| | Arg | Arg 50 | g Thr | : Let | ı Arg | , Gly | / His | Leu | ı Ala | a Lys | ; Il∈ | туі 60 | Ala | a Met | : His | s Trp |
| 20 | Ala 65 | Sei | Asp | Ser | Arg | Asn 70 | Leu | Val | Ser | Ala | Ser | Gln | . Asp | Gly | ' Lys | Leu 80 |
| 25 | Ile | Val | . Trp | Asp | 61y 85 | Tyr | Thr | Thr | Asn | Lys 90 | Val | His | Ala | Ile | Pro | Leu |
| | Arg | Ser | Ser | Trp | Val | Met | Thr | Cys | Ala 105 | Tyr | Ala | Pro | Ser | Gly 110 | Asn | Tyr |
| 30 | Val | Ala | Cys 115 | Gly | Gly | Leu | Asp | Asn 120 | Ile | Cys | Ser | Ile | Tyr 125 | Ser | Leu | Lys |
| | Thr | Arg 130 | Glu | Gly | Asn | Val | Arg 135 | Val | Ser | Arg | Glu | Leu 140 | Pro | Gly | His | Thr . |
| 35 | Gly 145 | Tyr | Leu | Ser | Cys | Cys 150 | Arg | Phe | Ile | Asp | Asp 155 | Asn | Gln | Ile | Val | Thr 160 |
| 40 | Ser | Ser | Gly | Asp | Met 165 | Thr | Cys | Ala | Leu | Trp 170 | Asn | Ile | Glu | Thr | Gly 175 | Asn |
| | Gln | Ile | Thr | Ser 180 | Phe | Gly | Gly | His | Thr 185 | Gly | Asp | Val | Met | Ser 190 | Leu | Ser |
| 45 | Leu | Ala | Pro 195 | Asp | Met | Arg | | Phe 200 | Val | Ser | Gly | | Cys 205 | Asp | Ala | Ser |

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|----|--|
| | Ala Lys Leu Phe Asp Ile Arg Asp Gly Ile Cys Lys Gln Thr Phe Thr 210 215 220 |
| 5 | Gly His Glu Ser Asp Ile Asn Ala Ile Thr Tyr Phe Pro Asn Gly Phe 225 230 235 240 |
| | Ala Phe Ala Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp Ile 245 250 255 |
| 10 | Arg Ala Asp Gln Glu Ile Gly Met Tyr Ser His Asp Asn Ile Ile Cys 260 265 270 |
| | Gly Ile Thr Ser Val Ala Phe Ser Lys Ser Gly Arg Leu Leu Gly 275 280 285 |
| 15 | Gly Tyr Asp Asp Phe Asn Cys Asn Val Trp Asp Val Leu Lys Gln Glu 290 295 300 |
| 20 | Arg Ala Gly Val Leu Ala Gly His Asp Asn Arg Val Ser Cys Leu Gly 305 310 315 320 |
| | Val Thr Glu Asp Gly Met Ala Val Ala Thr Gly Ser Trp Asp Ser Phe 325 330 335 |
| 25 | Leu Lys Ile Trp Asn 340 |
| | (2) INFORMATION FOR SEQ ID NO:46: |
| 30 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 410 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| 35 | (ii) MOLECULE TYPE: protein |
| • | (iii) HYPOTHETICAL: NO |
| | (iv) ANTI-SENSE: NO |
| 40 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: IEF SSP 9306, Fig. 29</pre> |

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

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| | Me 1 | et A | la A | sp : | | Glu 5 | Ala | Alá | a Ph | ie As | | sp A | ala v | al (| Slu | Glu | Arg 15 | Val |
|----|------------|------------|------------|-----------|------------|------------|------------------------|--------------|------------|------------------------|------------|-------------|--------------|------------|------------|------------|-----------|-----------|
| 5 | 11 | le A | sn G | lu (| Slu ' | Tyr | Lys | Ile | e Tr | p L _} 25 | | ys A | sn T | hr P | | Phe 30 | Leu | Tyr |
| | As | p Le | eu V 3 | al M 5 | let : | Thr : | His | Ala | 40 | u Gl | u T | rp P | ro S | er L 4 | | hr . | Ala | Gln |
| 10 | Tr | p Le 50 | eu P: | ro A | sp V | al ' | Thr | Arg 55 | Pro | Gl | u G | ly Ly | ys A: 60 | spPi | ne S | er 1 | le | His |
| 15 | Ar 65 | g Le | u Va | al L | eu G | ly 1 | Thr 70 | His | Thr | : Se: | r As | sp G] 75 | | .n As | n H | is L | | Val 80 |
| | Ile | ∋ Al | a Se | er Va | al G 8 | ln I 5 | eu : | Pro | Asn | Ası | 90 | | a Gl | n Ph | e A | sp A 9 | | Ser |
| 20 | His | ту | r As | p Se | er G | lu L | ys (| Gly | Glu | Phe | | y Gl | y Ph | e Gl | y Se | | al S | Ser |
| | Gly | Ly: | 3 Il 11 | e Gl 5 | u I | Le G | lu] | | Lys 120 | Ile | Ası | n Hi | s Gl | u Gl: | | u Vá | al A | sn |
| 25 | Arg | Ala 130 | a Arg | у Ту | r Me | t Pi | | Sln . .35 | Asn | Pro | Cys | 5 Ile | ⊇ Ile 140 | ⊇ Ala | a Th | r Ly | 's T | hr |
| 30 | Pro 145 | Ser | Sei | As; | p Va | l Le 15 | ∋u V | al : | Phe | Asp | Туг | Thr 155 | | His | Pr | o Se | | ys 60 |
| | Pro | Asp | Pro | Se: | r Gl 16 | y G1 5 | u C | ys 1 | Asn | Pro | Asp 170 | | Arg | Leu | Ar | g Gl 17 | | is |
| 35 | Gln | Lys | Glu | 180 | / Ty: | r Gl | y L | eu S | | Trp 185 | Asn | Pro | Asn | Leu | Ser 190 | | y Hi | .s |
| | Leu | Leu | Ser 195 | Ala | Se: | As | p As | | is ' | Thr | Ile | Cys | Leu | Trp 205 | Asp | Ile | e Se | r |
| 40 | Ala | Val 210 | Pro | Lys | Glı | ı Gl | y L ₃ 21 | | al v | /al | Asp | Ala | Lys 220 | Thr | Ile | Phe | : Th | r |
| 45 | Gly 225 | His | Thr | Ala | Va] | . Va: | 1 G1 | u A | sp 7 | /al | Ser | Trp 235 | His | Leu | Leu | His | G1 24 | |
| | Ser | Leu | Phe | Gly | Ser | Va] | l Al | a A | sp A | Asp (| Gln | Lys | Leu | Met | Ile | Trp | As | p |

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255 250 245 Thr Arg Ser Asn Asn Thr Ser Lys Pro Ser His Ser Val Asp Ala His 265 260 5 Thr Ala Glu Val Asn Cys Leu Ser Phe Asn Pro Tyr Ser Glu Phe Ile 275 Leu Ala Thr Gly Ser Ala Asp Lys Thr Val Ala Leu Trp Asp Leu Arg 10 Asn Leu Lys Leu Lys Leu His Ser Phe Glu Ser His Lys Asp Glu Ile 315 310 305 Phe Gln Val Gln Trp Ser Pro His Asn Glu Thr Ile Leu Ala Ser Ser 15 330 325 Gly Thr Asp Arg Arg Leu Asn Val Trp Asp Leu Ser Lys Ile Gly Glu 345 340 20 Glu Gln Ser Pro Glu Asp Ala Glu Asp Gly Pro Pro Glu Leu Leu Phe 360 355 Ile His Gly Gly His Thr Ala Lys Ile Ser Asp Phe Ser Trp Asn Pro 380 375 370 25 Asn Glu Pro Trp Val Ile Cys Ser Val Ser Glu Asp Asn Ile Met Gln 395 390 385 Val Trp Gln Met Glu Leu Val Leu Asp His 30.... 410 405 (2) INFORMATION FOR SEQ ID NO:47: (i) SEQUENCE CHARACTERISTICS: 35 (A) LENGTH: 317 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 40

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

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(C) INDIVIDUAL ISOLATE: HUMAN 12.3, Fig. 30

| 5 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:47: |
|----|--|
| | Met Thr Glu Gln Met Thr Leu Arg Gly Thr Leu Lys Gly His Asn Gly 1 5 10 15 |
| 10 | Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro Asp Met Ile Leu 20 25 30 |
| | Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys Leu Thr Arg Asp 35 40 45 |
| 15 | Glu Thr Asn Tyr Gly Ile Pro Gln Arg Ala Leu Arg Gly His Ser His 50 55 60 |
| 20 | Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln Phe Ala Leu Ser 70 75 80 |
| | Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp Leu Thr Thr Gly Thr 85 90 95 |
| 25 | Thr Thr Arg Arg Phe Val Gly His Thr Lys Asp Val Leu Ser Val Ala |
| | Phe Ser Ser Asp Asn Arg Gln Ile Val Ser Gly Ser Arg Asp Lys Thr 115 120 125 |
| 30 | Ile Lys Leu Trp Asn Thr Leu Gly Val Cys Lys Tyr Thr Val Gln Asp 130 135 140 |
| 35 | Glu Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser 145 150 155 160 |
| | Ser Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val 165 170 175 |
| 40 | Trp Asn Leu Ala Asn Cys Lys Leu Lys Thr Asn His Ile Gly His Thr 180 185 190 |
| | Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser Leu Cys Ala 195 200 205 |
| 45 | Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp Leu Asn Glu Gly 210 215 220 |

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| | - 120 - |
|------|--|
| | Lys His Leu Tyr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys 235 230 235 |
| 5 | Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile 245 250 255 |
| | Lys Ile Trp Asp Leu Glu Gly Lys Ile Ile Val Asp Glu Leu Lys Gln 260 265 270 |
| 10 | Glu Val Ile Ser Thr Ser Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser 275 280 285 |
| | Leu Ala Trp Ser Ala Asp Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp 290 295 300 |
| 15 | Asn Leu Val Arg Val Trp Gln Val Thr Ile Gly Thr Arg 305 310 315 |
| (2) | INFORMATION FOR SEQ ID NO:48: (i) SEQUENCE CHARACTERISTICS: |
| | (A) LENGTH: 425 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| 25 | (ii) MOLECULE TYPE: protein |
| | (iii) HYPOTHETICAL: NO |
| 30 | (iv) ANTI-SENSE: NO |
| •• : | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: IEF -7442 - human, Fig. 31</pre> |
| 35 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:48: |
| | Met Ala Ser Lys Glu Met Phe Glu Asp Thr Val Glu Glu Arg Val Ile 1 10 15 |
| 40 | Asn Glu Glu Tyr Lys Ile Trp Lys Lys Asn Thr Pro Phe Leu Tyr Asp 20 25 30 |
| 45 | Leu Val Met Thr His Ala Leu Gln Trp Pro Ser Leu Thr Val Gln Trp 35 40 45 |

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| | Leu Pro Glu Val Thr Lys Pro Glu Gly Lys Asp Tyr Ala Leu His Trp. 50 55 60 |
|----|--|
| 5 | Leu Val Leu Gly Thr His Thr Ser Asp Glu Gln Asn His Leu Val Val 65 70 75 80 |
| | Ala Arg Val His Ile Pro Asn Asp Asp Ala Gln Phe Asp Ala Ser His 85 90 95 |
| 10 | Cys Asp Ser Asp Lys Gly Glu Phe Gly Gly Phe Gly Ser Val Thr Gly 100 105 110 |
| 15 | Lys Ile Glu Cys Glu Ile Lys Ile Asn His Glu Gly Glu Val Asn Arg 115 120 125 |
| | Ala Arg Tyr Met Pro Gln Asn Pro His Ile Ile Ala Thr Lys Thr Pro 130 135 140 |
| 20 | Ser Ser Asp Val Leu Val Phe Asp Tyr Thr Lys His Pro Ala Lys Pro 145 150 155 160 |
| | Asp Pro Ser Gly Glu Cys Asn Pro Asp Leu Arg Leu Arg Gly His Gln 165 170 175 |
| 25 | Lys Glu Gly Tyr Gly Leu Ser Trp Asn Ser Asn Leu Ser Gly His Leu 180 185 190 |
| 30 | Leu Ser Ala Ser Asp Asp His Thr Val Cys Leu Trp Asp Ile Asn Ala 195 200 205 |
| | Gly Pro Lys Glu Gly Lys Ile Val Asp Ala Lys Ala Ile Phe Thr Gly 210 220 |
| 35 | His Ser Ala Val Val Glu Asp Val Ala Trp His Leu Leu His Glu Ser 230 235 240 |
| | Leu Phe Gly Ser Val Ala Asp Asp Gln Lys Leu Met Ile Trp Asp Thr 245 250 255 |
| 40 | Arg Ser Asn Thr Thr Ser Lys Pro Ser His Leu Val Asp Ala His Thr 260 265 270 |
| 45 | Ala Glu Val Asn Cys Leu Ser Phe Asn Pro Tyr Ser Glu Phe Ile Leu 275 280 285 |
| | Ala Thr Gly Ser Ala Asp Lys Thr Val Ala Leu Trp Asp Leu Arg Asn |

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Leu Lys Leu Lys Leu His Thr Phe Glu Ser His Lys Asp Glu Ile Phe 305 310 315 320

Gln Val His Trp Ser Pro His Asn Glu Thr Ile Leu Ala Ser Ser Gly
325 330 335

Thr Asp Arg Leu Asn Val Trp Asp Leu Ser Lys Ile Gly Glu Glu
10 340 345 350

Gln Ser Ala Glu Asp Ala Glu Asp Gly Pro Pro Glu Leu Leu Phe Ile 355 360 365

His Gly Gly His Thr Ala Lys Ile Ser Asp Phe Ser Trp Asn Pro Asn 370 375 380

Glu Pro Trp Val Ile Cys Ser Val Ser Glu Asp Asn Ile Met Gln Ile 385 390 395 400

20
Trp Gln Met Ala Glu Asn Ile Tyr Asn Asp Glu Glu Ser Asp Val Thr
405
410
415

Thr Ser Glu Leu Glu Gly Gln Gly Ser

- (2) INFORMATION FOR SEQ ID NO:49:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 605 amino acids

(B) TYPE: amino acid(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

(iii) HYPOTHETICAL: NO

30-

35

(iv) ANTI-SENSE: NO

- 40 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: Insulin-like growth factor binding protein complex, Fig. 32
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

45 Met Ala Leu Arg Lys Gly Gly Leu Ala Leu Leu Leu Leu Ser

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| | 1 5 | 10 | 15 |
|-----|------------------------------------|---|-------------------|
| 5 | Trp Val Ala Leu Gly Pro 20 | Arg Ser Leu Glu Gly Ala Asp 25 | Pro Gly Thr |
| | Pro Gly Glu Ala Glu Gly 35 | Pro Ala Cys Pro Ala Ala Cys 40 45 | Val Cys Ser |
| 10 | Tyr Asp Asp Asp Ala Asp | Glu Leu Ser Val Phe Cys Ser 55 60 | Ser Arg Asn |
| | Leu Thr Arg Leu Pro Asp (| Gly Val Pro Gly Gly Thr Gln 75 | Ala Leu Trp 80 |
| 15 | Leu Asp Gly Asn Asn Leu S 85 | Ser Ser Val Pro Pro Ala Ala : 90 | Phe Gln Asn 95 |
| 20 | 100 | • | 110 |
| | **3 | eu Gly Leu Glu Asn Leu Cys H 120 125 | |
| 25 | 13 | 140 | |
| 7.0 | | eu Gly Leu Ser Asn Asn Arg Le 155 | 160 |
| 30 | | u Gly Leu Gly Ser Leu Trp As 170 | 175 |
| 35 | 100 | a Val Leu Pro Asp Ala Ala Ph 185 19 | 0 |
| | 222 | val Leu Ala Gly Asn Arg Le 200 205 | |
| 40 | 215 | 220 | |
| 45 | 230 | Ala Ile Lys Ala Asn Val Phe 235 | 240 |
| ~J | Leu Pro Arg Leu Gln Lys Leu 245 | Tyr Leu Asp Arg Asn Leu Ile 250 | Ala Ala 255 |

| | - 124 - |
|-----|---|
| | Val Ala Pro Gly Ala Phe Leu Gly Leu Lys Ala Leu Arg Trp Leu Asp 260 265 270 |
| 5 | Leu Ser His Asn Arg Val Ala Gly Leu Leu Glu Asp Thr Phe Pro Gly 275 280 285 |
| | Leu Leu Gly Leu Arg Val Leu Arg Leu Ser His Asn Ala Ile Ala Ser 290 295 300 |
| 10 | Leu Arg Pro Arg Thr Phe Lys Asp Leu His Phe Leu Glu Glu Leu Gln 305 310 315 320 |
| | Leu Gly His Asn Arg Ile Arg Gln Leu Ala Glu Arg Ser Phe Glu Gly 325 330 335 |
| 15. | Leu Gly Gln Leu Glu Val Leu Thr Leu Asp His Asn Gln Leu Gln Glu 340 345 350 |
| 20 | Val Lys Ala Gly Ala Phe Leu Gly Leu Thr Asn Val Ala Val Met Asn 355 360 365 |
| | Leu Ser Gly Asn Cys Leu Arg Asn Leu Pro Glu Gln Val Phe Arg Gly 370 375 380 |
| 25 | Leu Gly Lys Leu His Ser Leu His Leu Glu Gly Ser Cys Leu Gly Arg 395 400 |
| | Ile Arg Pro His Thr Phe Thr Gly Leu Ser Gly Leu Arg Arg Leu Phe 405 410 415 |
| 30 | Leu Lys Asp Asn Gly Leu Val Gly Ile Glu Glu Gln Ser Leu Trp Gly 420 425 430 |
| 35 | Leu Ala Glu Leu Leu Glu Leu Asp Leu Thr Ser Asn Gln Leu Thr His 435 440 445 |
| | Leu Pro His Arg Leu Phe Gln Gly Leu Gly Lys Leu Glu Tyr Leu Leu 450 455 460 |
| 40 | Leu Ser Arg Asn Arg Leu Ala Glu Leu Pro Ala Asp Ala Leu Gly Pro 465 470 475 480 |
| | Leu Gln Arg Ala Phe Trp Leu Asp Val Ser His Asn Arg Leu Glu Ala 485 490 495 |
| 45 | Leu Pro Asn Ser Leu Leu Ala Pro Leu Gly Arg Leu Arg Tyr Leu Ser |

45

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500 505 510 Leu Arg Asn Asn Ser Leu Arg Thr Phe Thr Pro Gln Pro Pro Gly Leu 515 520 5 Glu Arg Leu Trp Leu Glu Gly Asn Pro Trp Asp Cys Gly Cys Pro Leu 530 535 Lys Ala Leu Arg Asp Phe Ala Leu Gln Asn Pro Ser Ala Val Pro Arg 10 550 555 560 Phe Val Gln Ala Ile Cys Glu Gly Asp Asp Cys Gln Pro Pro Ala Tyr 570 15 Thr Tyr Asn Asn Ile Thr Cys Ala Ser Pro Pro Glu Val Val Gly Leu 585 590 Asp Leu Arg Asp Leu Ser Glu Ala His Phe Ala Pro Cys 600 605 20 (2) INFORMATION FOR SEQ ID NO:50: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 603 amino acids 25 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 30 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 35 (C) INDIVIDUAL ISOLATE: Insulin-like growth factor bind. pro. complex-rat, Fig. 33 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:50: 40 Met Ala Leu Arg Thr Gly Gly Pro Ala Leu Val Val Leu Leu Ala Phe 10 Trp Val Ala Leu Gly Pro Cys His Leu Gln Gly Thr Asp Pro Gly Ala 20 25 30 Ser Ala Asp Ala Glu Gly Pro Gln Cys Pro Val Ala Cys Thr Cys Ser

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| | - 126 - |
|----|---|
| | 35 4 0 4 5 |
| | His Asp Asp Tyr Thr Asp Glu Leu Ser Val Phe Cys Ser Ser Lys Asn 50 55 60 |
| 5 | Leu Thr His Leu Pro Asp Asp Ile Pro Val Ser Thr Arg Ala Leu Trp 65 70 75 80 |
| 10 | Leu Asp Gly Asn Asn Leu Ser Ser Ile Pro Ser Ala Ala Phe Gln Asn 90 95 |
| | Leu Ser Ser Leu Asp Phe Leu Asn Leu Gln Gly Ser Trp Leu Arg Ser 100 105 110 |
| 15 | Leu Glu Pro Gln Ala Leu Leu Gly Leu Gln Asn Leu Tyr Tyr Leu His 115 120 125 |
| | Leu Glu Arg Asn Arg Leu Arg Asn Leu Ala Val Gly Leu Phe Thr His 130 140 |
| 20 | Thr Pro Ser Leu Ala Ser Leu Ser Leu Ser Ser Asn Leu Leu Gly Arg 145 150 155 160 |
| 25 | Leu Glu Glu Gly Leu Phe Gln Gly Leu Ser His Leu Trp Asp Leu Asn 175 165 170 175 |
| | Leu Gly Trp Asn Ser Leu Val Val Leu Pro Asp Thr Val Phe Gln Gly 180 185 190 |
| 30 | Leu Gly Asn Leu His Glu Leu Val Leu Ala Gly Asn Lys Leu Thr Tyr 195 200 205 |
| | Leu Gln Pro Ala Leu Phe Cys Gly Leu Gly Glu Leu Arg Glu Leu Asp 210 215 220 |
| 35 | Leu Ser Arg Asn Ala Leu Arg Ser Val Lys Ala Asn Val Phe Val His 225 230 235 240 |
| 40 | Leu Pro Arg Leu Gln Lys Leu Tyr Leu Asp Arg Asn Leu Ile Thr Ala 245 250 255 |
| | Val Ala Pro Gly Ala Phe Leu Gly Met Lys Ala Leu Arg Trp Leu Asp 260 265 270 |
| 45 | Leu Ser His Asn Arg Val Ala Gly Leu Met Glu Asp Thr Phe Pro Gly 285 |

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| | Leu Leu Gly Leu His Val Leu Arg Leu Ala His Asn Ala Ile Ala Ser 290 295 300 |
|----|---|
| 5 | Leu Arg Pro Arg Thr Phe Lys Asp Leu His Phe Leu Glu Glu Leu Gln 305 310 315 320 |
| | Leu Gly His Asn Arg Ile Arg Gln Leu Gly Glu Arg Thr Phe Glu Gly 325 330 335 |
| 10 | Leu Gly Gln Leu Glu Val Leu Thr Leu Asn Asp Asn Gln Ile Thr Glu 340 345 350 |
| 15 | Val Arg Val Gly Ala Phe Ser Gly Leu Phe Asn Val Ala Val Met Asn 355 360 365 |
| | Leu Ser Gly Asn Cys Leu Arg Ser Leu Pro Glu Arg Val Phe Gln Gly 370 375 380 |
| 20 | Leu Asp Lys Leu His Ser Leu His Leu Glu His Ser Cys Leu Gly His 385 390 395 400 |
| | Val Arg Leu His Thr Phe Ala Gly Leu Ser Gly Leu Arg Arg Leu Phe 405 410 415 |
| 25 | Leu Arg Asp Asn Ser Ile Ser Ser Ile Glu Glu Gln Ser Leu Ala Gly 420 425 430 |
| 30 | Leu Ser Glu Leu Leu Glu Leu Asp Leu Thr Thr Asn Arg Leu Thr His 435 440 445 |
| | Leu Pro Arg Gln Leu Phe Gln Gly Leu Gly His Leu Glu Tyr Leu Leu 450 455 460 |
| 35 | Leu Ser Tyr Asn Gln Leu Thr Thr Leu Ser Ala Glu Val Leu Gly Pro 465 470 475 480 |
| | Leu Gln Arg Ala Phe Trp Leu Asp Ile Ser His Asn His Leu Glu Thr 485 490 495 |
| 40 | Leu Ala Glu Gly Leu Phe Ser Ser Leu Gly Arg Val Arg Tyr Leu Ser 500 505 510 |
| 45 | Leu Arg Asn Asn Ser Leu Gln Thr Phe Ser Pro Gln Pro Gly Leu Glu 515 520 525 |
| | Arg Leu Trp Leu Asp Ala Asn Pro Trp Asp Cys Ser Cys Pro Leu Lys |

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540 535 530

Ala Leu Arg Asp Phe Ala Leu Gln Asn Pro Gly Val Val Pro Arg Phe 555 550

Val Gln Thr Val Cys Glu Gly Asp Asp Cys Gln Pro Val Tyr Thr Tyr 5 570

Asn Asn Ile Thr Cys Ala Gly Pro Ala Asn Val Ser Gly Leu Asp Leu 590 585 580 10

> Arg Asp Val Ser Glu Thr His Phe Val His Cys 595

15... (2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 409 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown 20

- (ii) MOLECULE TYPE: protein
- (iii) HYPOTHETICAL: NO

25

- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: LIS1 (human), Fig. 34

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- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:
- Met Val Leu Ser Gln Arg Gln Arg Asp Glu Leu Asn Arg Ala Ile Ala 10 35

Asp Tyr Leu Arg Ser Asn Gly Tyr Glu Glu Ala Tyr Ser Val Phe Lys 25

- Lys Glu Ala Glu Leu Asp Val Asn Glu Glu Leu Asp Lys Lys Tyr Ala 40 40 35
 - Gly Leu Leu Glu Lys Lys Trp Thr Ser Val Ile Arg Leu Gln Lys Lys 60 55 50

Val Met Glu Leu Glu Ser Lys Leu Asn Glu Ala Lys Glu Glu Phe Thr 45

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| | 65 | 5 | | | | 70 |) | | | | 75 | i | | | | 80 | |
|----|------------|------------|--------------|--------------|------------|------------|--------------|------------|------------|------------|--------------|-----------------|------------|------------|-------------------|---------------------|---|
| 5 | Se | er Gl | y Gl | y Pro | 5 Le 85 | u Gl | y Gl | n Ly | s Ar | g As | | o Ly | s Gl | u Tr | p II 99 | le Pr | 0 |
| | Ar | g Pr | o Pr | 0 Gli 100 | ı Ly | s Ty | r Ala | a Le | u Se 10 | | y Hi | s Ar | g Se | r Pr 11 | | ıl Th: | r |
| 10 | Ar | g Va | 1 Ile 11: | e Phe | Hi: | s Pro | o Val | l Phe | | r Va | l Me | t Vai | l Se: | | a Se | r Glı | 1 |
| | Asj | p Ala | a Thi | r Ile | . Lys | s Val | l Trp 135 | | ту: | r Gli | ı Thr | Gl ₃ | | ⊃ Ph€ | e Gl | u Arg | ř |
| 15 | Th: | r Lei | ı Lys | Gly | His | 150 | | Ser | Val | Glr | 1 Asp | | : Ser | Phe | e As _l | 9 His 160 | |
| 20 | Sei | Gly | / Lys | Leu | Leu 165 | Ala | Ser | . Cys | Ser | 170 | | Met | Thr | Ile | Lys | Leu | |
| | Trp | Asp | Phe | Gln 180 | Gly | Phe | Glu | Суз | Ile 185 | | Thr | Met | His | Gly 190 | | Asp | |
| 25 | His | Asn | Val 195 | Ser | Ser | Val | Ala | Ile 200 | Met | Pro | Asn | Gly | Asp 205 | His | Ile | Val | |
| | Ser | Ala 210 | Ser | Arg | Asp | Lys | Thr 215 | Ile | Lys | Met | Trp | Glu 220 | Val | Gln | Thr | Gly | |
| 30 | Tyr 225 | Cys | Val | Lys | Thr | Phe 230 | Thr | Gly | His | Arg | Glu 235 | Trp | Val | Arg | Met | Val 240 | |
| 35 | Arg | Pro | Asn | Gln | Asp 245 | Gly | Thr | Leu | Ile | Ala 250 | Ser | Cys | Ser | Asn | Asp 255 | Gln | |
| | Thr | Val | Arg | Val 260 | Trp | Val | Val | | Thr 265 | Lys | Glu | Cys | | Ala 270 | Glu | Leu | |
| 40 | Arg | Glu | His 275 | Glu : | His | Val | | Glu 280 | Cys | Ile | Ser | | Ala 285 | Pro | Glu | Ser | |
| | Ser | Tyr 290 | Ser | Ser | Ile | | Glu 295 | Ala | Thr | Gly | | Glu 300 | Thr | Lys | Lys | Ser | |
| 45 | Gly 305 | Lys | Pro | Gly 1 | Pro | Phe 310 | Leu | Leu | Ser | | Ser . 315 | Arg . | Asp : | Lys | | Lys 320 | |

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|----------------|--|
| | Met Trp Asp Val Ser Thr Gly Met Cys Leu Met Thr Leu Val Gly His 325 330 335 |
| 5 | Asp Asn Trp Val Arg Gly Val Leu Phe His Ser Gly Gly Lys Phe Ile 340 345 350 |
| | Leu Ser Cys Ala Asp Asp Lys Thr Leu Arg Val Trp Asp Tyr Lys Asn 355 360 365 |
| 10 | Lys Arg Cys Met Lys Thr Leu Asn Ala His Glu His Phe Val Thr Ser 370 375 380 |
| | Leu Asp Phe His Lys Thr Ala Pro Tyr Val Val Thr Gly Ser Val Asp 385 390 395 400 |
| 15 | Gln Thr Val Lys Val Trp Glu Cys Arg 405 |
| 20 | (2) INFORMATION FOR SEQ ID NO:52: |
| | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 422 amino acids(B) TYPE: amino acid |
| 25 | (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein |
| | (iii) HYPOTHETICAL: NO |
| 30 | (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: |
| 35 | (C) INDIVIDUAL ISOLATE: MD6, Fig. 35 |
| 33 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:52: Met Glu Arg Lys Asp Phe Glu Thr Trp Leu Asp Asn Ile Ser Val Thr |
| 40 | 1 5 10 15 |
| - - | Phe Leu Ser Leu Met Asp Leu Gln Lys Asn Glu Thr Leu Asp His Leu 20 25 30 |
| 45 | Ile Ser Leu Ser Gly Ala Val Gln Leu Arg His Leu Ser Asn Asn Leu 35 40 45 |

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| | GI | u T | nr L | eu L | eu I | ys . | Arg | Asp 55 | Ph | e L | eu L | ys I | | Leu 60 | Pro | o Le | eu G | lu | Leu |
|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------|-----------|-------------------|------------|------------|------|-----------|
| 5 | Se 65 | r Pł | ne T | yr L | eu L | | Lys 70 | Trp | Le | u As | sp P | | ln ' | Thr | Leu | ı Le | u T | hr | Cys 80 |
| | Су | s Le | eu Va | al S | er L 8 | ys (5 | 3ln | Arg | Ası | n Ly | rs Va | | le s | Ser | Ala | Сy | s T) | | Glu |
| 10 | Va. | l Tr | p Gl | n Th | nr Ai | la C | :ys | Lys | Asr | Le 10 | | Ly T: | rp G | Iln | Ile | Asp | | sp : | Ser |
| 15 | Val | . Gl: | n As 11 | p Se 5 | r Le | eu H | is | Trp | Lys 120 | Ly | s Va | а ту | r L | | Lys 125 | Ala | ıIl | e I | Leu |
| | Arg | Met | t Ly | s Gl | n Le | u G | lu : | Asp 135 | His | Glı | ı Al | a Ph | | lu 7 | Thr | Ser | Se | r L | eu |
| 20 | Ile 145 | Gl | / Hi: | s Se: | r Al | a A: | rg 7 50 | /al | Tyr | Ala | ı Lei | u Ty 15 | | yr L | ys | Asp | Gl | | eu 60 |
| | Leu | Cys | Thi | Gly | y Se: | r As | sp A | Asp | Leu | Ser | Ala 170 | | s Le | u T | rp . | Asp | Va] | | er |
| 25 | Thr | Gly | Glr | Cys | s Val | ι ту | r G | ly : | | Gln 185 | Thr | His | 5 Th | r C | | Ala L90 | Ala | . Va | al |
| 30 | Lys | Phe | Asp 195 | Glu | Glr | Ly | s L | eu V | /al 200 | Thr | Gly | Ser | Ph | | sp <i>F</i> 05 | Asn | Thr | Va | ıl |
| 30 | Ala | Cys 210 | Trp | Glu | Trp | Se: | | er 0 | Sly : | Ala | Arg | Thr | Gl: | | ls P | he . | Arg | Gl | У |
| 35 | His 225 | Thr | Gly | Ala | Val | Phe 230 | ≘ Se | er V | al 1 | Asp | туг | Ser 235 | Asp | o Gl | u L | eu i | Asp | Il: | |
| | Leu | Val | Ser | Gly | Ser 245 | Ala | a As | p P | he A | | Val 250 | Lys | Val | Tr | p A | | Leu 255 | Sei | r |
| 40 | Ala | 3ly | Thr | Cys 260 | Leu | Asn | 1 Th | ır L | | hr 65 | Gly | His | Thr | Gl: | | rp V 70 | al' | Thr | : |
| 45 | Lys \ | /al | Val 275 | Leu | Gln | Lys | Су | s Ly 20 | ys V 30 | al : | Lys | Ser | Leu | Le: | | is S | er | Pro |) |
| | Gly A | sp ' | Tyr | Ile | Leu | Leu | Se | r Al | la A | .sp 1 | Lys | Tyr | Glu | Ile | ∍ Ly | s I | le ' | Trp | , |

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290 295 300

Pro Ile Gly Arg Glu Ile Asn Cys Lys Cys Leu Lys Thr Leu Ser Val 305 310 315 320

5

Ser Glu Asp Arg Ser Ile Cys Leu Gln Pro Arg Leu His Phe Asp Gly 325 330 335

Lys Tyr Ile Val Cys Ser Ser Ala Leu Gly Leu Tyr Gln Trp Asp Phe
340 345 350

Ala Ser Tyr Asp Ile Leu Arg Val Ile Lys Thr Pro Glu Val Ala Asn 355 360 365

Leu Ala Leu Leu Gly Phe Gly Asp Val Phe Ala Leu Leu Phe Asp Asn 370 375 380

His Tyr Leu Tyr Ile Met Asp Leu Arg Thr Glu Ser Leu Ile Ser Arg 385 390 395 400

20

25

Trp Pro Leu Pro Glu Tyr Arg Lys Ser Lys Arg Gly Thr Ser Phe Leu 405 410 415

Ala Gly Glu Arg Pro Gly 420

- (2) INFORMATION FOR SEQ ID NO:53:
 - (i) SEQUENCE CHARACTERISTICS:

30. (A) LENGTH: 422 amino acids

- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: protein

35

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 40 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: MSL1, Fig. 36
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

45 Met Asn Gln Cys Ala Lys Asp Ile Thr His Glu Ala Ser Ser Ile Pro

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| | 1 | ! | 5 | 10 | 15 |
|----|----------------|---------------------|---------------------|------------------------------------|------------------------|
| 5 | Ile A | asp Leu Gln (| Glu Arg Tyr | Ser His Trp Lys Lys 25 | Asn Thr Lys Leu |
| | Leu T | yr Asp Tyr I 35 | | Asn Ser Thr Lys Trp 40 | Pro Ser Leu Thr |
| 10 | Cys G. | ln Phe Phe P O | ro Asp Leu . 55 | Asp Thr Thr Ser Asp | Glu His Arg Ile |
| | Leu Le | eu Ser Ser P | he Thr Ser § | Ger Gln Lys Pro Glu 75 | Asp Glu Thr Ile |
| 15 | Tyr Il | e Ser Lys II. 85 | le Ser Thr I | eu Gly His Ile Lys 90 | Trp Ser Ser Leu 95 |
| 20 | | 100 | | et Glu Phe Lys Pro 105 | 110 |
| | Arg Ph | e Pro Ser Ly 115 | s His Leu V | al Asn Asp Ile Ser : 20 | Ile Phe Phe Pro 125 |
| 25 | Asn Gly | y Glu Cys As:) | n Arg Ala An 135 | rg Tyr Leu Pro Gln <i>I</i> 140 | asn Pro Asp Ile |
| | Ile Ala | d Gly Ala Ser | r Ser Asp Gl 150 | y Ala Ile Tyr Ile F 155 | he Asp Arg Thr 160 |
| 30 | Lys His | Gly Ser Thr | Arg Ile Ar | g Gln Ser Lys Ile S 170 | er His Pro Phe 175 |
| 35 | | 180 | | s Gly Val Ile Gln A | 190 |
| | | 193 | 200 | 20 | 05 |
| 40 | Asn Leu 210 | Gln Gln Glu | Ala Leu Leu 215 | ı Leu Ser Ser His Se 220 | r Asn Gly Gln |
| | 223 | | 230 | Tyr Ser His Glu As 235 | 240 |
| 45 | Asp Leu | Pro Leu Val 245 | Ser Ile Asn | Ser Asp Gly Thr Al | a Val Asn Asp |

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| | The Ala Cys Thr Glu |
|------|---|
| | Val Thr Trp Met Pro Thr His Asp Ser Leu Phe Ala Ala Cys Thr Glu 260 265 270 |
| 5 | Gly Asn Ala Val Ser Leu Leu Asp Leu Arg Thr Lys Lys Glu Lys Leu 275 280 285 |
| | Gln Ser Asn Arg Glu Lys His Asp Gly Gly Val Asn Ser Cys Arg Phe 290 295 300 |
| 10 | Asn Tyr Lys Asn Ser Leu Ile Leu Ala Ser Ala Asp Ser Asn Gly Arg 305 310 315 320 |
| | Leu Asn Leu Trp Asp Ile Arg Asn Met Asn Lys Ser Pro Ile Ala Thr 325 330 335 |
| 15 | Met Glu His Gly Thr Ser Val Ser Thr Leu Glu Trp Ser Pro Asn Phe 340 345 350 |
| 20 | Asp Thr Val Leu Ala Thr Ala Gly Gln Glu Asp Gly Leu Val Lys Leu 355 360 365 |
| | Trp Asp Thr Ser Cys Glu Glu Thr Ile Phe Thr His Gly Gly His Met 370 375 380 |
| 25 | Leu Gly Val Asn Asp Ile Ser Trp Asp Ala His Asp Pro Trp Leu Met 385 390 395 400 |
| | Cys Ser Val Ala Asn Asp Asn Ser Val His Ile Trp Lys Pro Ala Gly 405 410 415 |
| 30 . | Asn Leu Val Gly His Ser 420 |
| | (2) INFORMATION FOR SEQ ID NO:54: |
| 35 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 816 amino acids |
| | (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| 40 | (ii) MOLECULE TYPE: protein |
| | (iii) HYPOTHETICAL: NO |

(iv) ANTI-SENSE: NO

45

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(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: MUS MUSCULUS PROTEIN, Fig. 37

| | Fig. 37 |
|----|--|
| 5 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:54: |
| | Phe Arg Met Asp Asn Ala Ser Thr Arg Ile Asp Glu Arg Phe Arg Ile 1 10 15 |
| 10 | Asp Ala Tyr Ala Asn Ala Arg Tyr Pro Met Pro Arg Thr Glu Ile Asn 20 25 30 |
| 15 | Ser Glu Gln Glu Asn Cys Glu Asn Thr Ile Thr Leu Glu Asp Ser Glu 35 40 45 |
| | Gln Glu Asn Cys Glu Ala Ala Cys Met Pro Leu Glu Thr Glu Ser Glu 50 55 60 |
| 20 | Gln Glu Asn Cys Glu Met Ser Ser His Glu Ser Tyr Thr Asn Ala Ala 65 70 75 80 |
| | Glu Thr Pro Glu Asn Ile Ser Ile Leu Ser Cys Leu Gly Glu Thr Ser 85 90 95 |
| 25 | Gly Ala Leu Val Asp Thr Lys Thr Ile Ser Asp Ile Lys Thr Met Asp 100 105 110 |
| 30 | Pro Arg Val Ser Leu Thr Pro Ser Ser Asp Val Thr Gly Thr Glu Asp 115 120 125 |
| | Ser Ser Val Leu Thr Pro Gln Ser Thr Asp Val Asn Ser Val Asp Ser 130 135 140 |
| 35 | Tyr Gln Gly Tyr Glu Gly Asp Asp Asp Glu Glu Asp Asp Glu Asp 145 150 155 160 |
| | Asp Lys Asp Gly Asp Ser Asn Leu Pro Ser Leu Glu Asp Ser Asp Asn 165 170 175 |
| 40 | Phe Ile Ser Cys Leu Glu Asn Ser Tyr Ile Pro Gln Asn Val Glu Asn 180 185 190 |
| | Gly Glu Val Val Glu Glu Gln Ser Leu Gly Arg Arg Phe His Pro Tyr 195 200 205 |

Glu Leu Glu Ala Gly Glu Val Val Glu Gly Gln Gly Gly Ser Leu

205

200

45

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| | - 136 - | |
|----|--|---|
| | 210 215 220 | |
| | Phe Tyr Pro Tyr Glu Leu Glu Ala Gly Glu Val Val Glu Ala Gln Asn 225 230 235 240 | |
| 5 | Val Gln Asn Leu Phe His Arg Tyr Glu Leu Glu Glu Gly Glu Val Val 245 250 255 | |
| 10 | Glu Ala Gln Val Val Gln Ser Met Phe Pro Tyr Tyr Glu Leu Glu Ala 260 265 270 | |
| | Gly Glu Val Val Glu Ala Glu Glu Val Gln Gly Phe Phe Gln Arg Tyr 275 280 285 | |
| 15 | Glu Leu Glu Ala Arg Glu Val Ile Gly Ala Gln Gly Gln Gly Leu 290 295 300 | |
| | Ser Arg His Tyr Gly Leu Glu Gly Gly Glu Val Val Glu Ala Thr Ala 305 310 315 320 | |
| 20 | Val Arg Arg Leu Ile Gln His His Glu Leu Glu Glu Gly Glu Asp Val 325 330 335 | |
| 25 | Asp Asp Gln Glu Glu Ser Ser Glu Met His Glu Glu Thr Ser Glu Asp 340 345 350 | |
| | Ser Ser Glu Gln Tyr Asp Ile Glu Asp Asp Ser Leu Ile Asp Glu Trp 355 360 365 | |
| 30 | Ile Ala Leu Glu Thr Ser Pro Leu Pro Arg Pro Arg Trp Asn Val Leu 370 380 | |
| | Ser Ala Leu Arg Asp Arg Gln Leu Gly Ser Ser Gly Arg Phe Val Tyr 385 390 395 400 | |
| 35 | Glu Ala Cys Gly Ala Arg Leu Phe Val Gln Arg Phe Ser Leu Glu His 405 410 415 | |
| 40 | Val Phe Glu Gly His Ser Gly Cys Val Asn Thr Val His Phe Asn Gln 420 425 430 | |
| | His Gly Thr Leu Leu Ala Ser Gly Ser Asp Asp Leu Lys Val Ile Val 435 440 445 | |
| 45 | Trp Asp Trp Leu Lys Lys Arg Ser Val Leu Asn Phe Asp Ser Gly His | 3 |

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| | 46 | 5 | | | | 470 |) | | | | 47 | 5 | | | | p Ala 480 |
|----|-----|-------|--------------|--------------|--------------|-------|------|--------------|-------|--------------|-------|-------|------|--------------|------------|--------------|
| 5 | Ile | e Le | u Al | a Me | t Cys 485 | | Arg | j Asj | o Gl | y Glr 490 | | l Arg | g Va | l Ala | a Gl 49 | n Leu 5 |
| | Sei | r Al | a Va | 1 Ala 500 | | Thr | His | Met | 505 | | Arg | g Let | ı Va | 1 Lys 510 | | s Gly |
| 10 | Gl | / Ala | a Sei 519 | | Arg | Leu | Gly | Leu 520 | | ı Pro | Asp | Ser | 525 | | e Arg | g Phe |
| 15 | | 530 |) | | | | 535 | | | | | 540 | | | | g Gln |
| | 545 | | | | Ser | 550 | | | | | 555 | | | | | 560 |
| 20 | | | | | Thr 565 | | | | | 570 | | | | | 575 | |
| | | | | 580 | Gln | | | | 585 | | | | | 590 | | |
| 25 | | | 595 | | Val | | | 600 | | | | | 605 | | | |
| 30 | | 610 | | | Ser | | 615 | | | | | 620 | | | | |
| | 625 | | | | | 630 | | | | | 635 | | | | | 640 |
| 35 | | | | | Ser : | | | | | 650 | | | | | 655 | |
| 40 | | | | 660 | Arg i | | | | 665 | | | | | 670 | | |
| 40 | | | 675 | | Glu I | | (| 5 8 0 | | | | | 685 | | | |
| 45 | | 690 | | | Lys S | 6 | 95 | | | | | 700 | | | | |
| | Asp | Glu | Gly | Gly | Thr 1 | [le A | sn (| Cys | Ile . | Asp : | Ser : | His 1 | Pro | Tyr 1 | Leu | Pro |

- 138 -720 715 710 705 Val Leu Ala Ser Ser Gly Leu Asp His Glu Val Lys Ile Trp Ser Pro 725 5 Ile Ala Glu Pro Ser Lys Lys Leu Ala Gly Leu Lys Asn Val Ile Lys 745 Ile Asn Lys Leu Lys Arg Asp Asn Phe Thr Leu Arg His Thr Ser Leu 765 760 10 Phe Asn Asn Ser Met Leu Cys Phe Leu Met Ser His Val Thr Gln Ser 780 775 770 Asn Tyr Gly Arg Ser Trp Arg Gly Ile Arg Ile Asn Ala Gly Gly 15 795 790 785 Asp Phe Ser Asp Ser Ser Ser Ser Glu Glu Thr Asn Gln Glu Ser 810 805 20 (2) INFORMATION FOR SEQ ID NO:55: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 422 amino acids 25 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein 30 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: ORF RB1, Fig. 38 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:55: 40 Met Asn Gln Cys Ala Lys Asp Ile Thr His Glu Ala Ser Ser Ile Pro 10 5 Ile Asp Leu Gln Glu Arg Tyr Ser His Trp Lys Lys Asn Thr Lys Leu 30 20 45

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| | Leu Tyr Asp Tyr Leu Asn Thr Asn Ser Thr Lys Trp Pro Ser Leu Thr 35 40 45 |
|----|--|
| 5 | Cys Gln Phe Phe Pro Asp Leu Asp Thr Thr Ser Asp Glu His Arg Ile 50 55 60 |
| | Leu Leu Ser Ser Phe Thr Ser Ser Gln Lys Pro Glu Asp Glu Thr Ile 70 75 80 |
| 10 | Tyr Ile Ser Lys Ile Ser Thr Leu Gly His Ile Lys Trp Ser Ser Leu 85 90 95 |
| 15 | Asn Asn Phe Asp Met Asp Glu Met Glu Phe Lys Pro Glu Asn Ser Thr 100 105 110 |
| | Arg Phe Pro Ser Lys His Leu Val Asn Asp Ile Ser Ile Phe Phe Pro 115 120 125 |
| 20 | Asn Gly Glu Cys Asn Arg Ala Arg Tyr Leu Pro Gln Asn Pro Asp Ile 130 135 140 |
| 25 | Ile Ala Gly Ala Ser Ser Asp Gly Ala Ile Tyr Ile Phe Asp Arg Thr 145 150 155 160 |
| 23 | Lys His Gly Ser Thr Arg Ile Arg Gln Ser Lys Ile Ser His Pro Phe 165 170 175 |
| 30 | Glu Thr Lys Leu Phe Gly Ser His Gly Val Ile Gln Asp Val Glu Ala 180 185 190 |
| | Met Asp Thr Ser Ser Ala Asp Ile Asn Glu Ala Thr Ser Leu Ala Trp 195 200 205 Asn Leu Gla Cla Cla Cla Cla Cla Cla Cla Cla Cla C |
| 35 | Asn Leu Gln Glu Ala Leu Leu Leu Ser Ser His Ser Asn Gly Gln 210 215 220 Val Gln Val Tro Ass II - |
| 40 | Val Gln Val Trp Asp Ile Lys Gln Tyr Ser His Glu Asn Pro Ile Ile 235 230 235 240 Asp Leu Pro Leu Val Ser Ile |
| | Asp Leu Pro Leu Val Ser Ile Asn Ser Asp Gly Thr Ala Val Asn Asp 245 250 255 Val Thr Trp Met Pro Thy Tri |
| 45 | Val Thr Trp Met Pro Thr His Asp Ser Leu Phe Ala Ala Cys Thr Glu 260 265 270 Gly Asp Ala Val Ser Leu Leu Phe Ala Ala Cys Thr Glu |
| | Gly Asn Ala Val Ser Leu Leu Asp Leu Arg Thr Lys Lys Glu Lys Leu |

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280 275 Gln Ser Asn Arg Glu Lys His Asp Gly Gly Val Asn Ser Cys Arg Phe 300 295 290 Asn Tyr Lys Asn Ser Leu Ile Leu Ala Ser Ala Asp Ser Asn Gly Arg 5 315 310 305 Leu Asn Leu Trp Asp Ile Arg Asn Met Asn Lys Ser Pro Ile Ala Thr 335 330 325 10 Met Glu His Gly Thr Ser Val Ser Thr Leu Glu Trp Ser Pro Asn Phe 345 340 Asp Thr Val Leu Ala Thr Ala Gly Gln Glu Asp Gly Leu Val Lys Leu 15 ... 365 360 355 Trp Asp Thr Ser Cys Glu Glu Thr Ile Phe Thr His Gly Gly His Met 375 370 Leu Gly Val Asn Asp Ile Ser Trp Asp Ala His Asp Pro Trp Leu Met 20 395 390 385 Cys Ser Val Ala Asn Asp Asn Ser Val His Ile Trp Lys Pro Ala Gly 410 405 25

Asn Leu Val Gly His Ser 420

30 - (2) INFORMATION FOR SEQ ID NO:56:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 576 amino acids
 - (B) TYPE: amino acid
- (D) TOPOLOGY: unknown 35
 - (ii) MOLECULE TYPE: protein
 - (iii) HYPOTHETICAL: NO
- 40
- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: Periodic Trp protein, Fig. 39

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

| 5 | Met Ile Ser Ala Thr Asn Trp Val Pro Arg Gly Phe Ser Ser Glu Phe 1 5 10 15 . Pro Glu Lys Tyr Val Leu Asp Asp Glu Glu Val Glu Arg Ile Asn Gln 20 25 30 |
|----|---|
| 10 | Leu Ala Gln Leu Asn Leu Asp Asp Ala Lys Ala Thr Leu Glu Glu Ala 35 40 45 |
| | Glu Gly Glu Ser Gly Val Glu Asp Asp Ala Ala Thr Gly Ser Ser Asn 50 55 60 |
| 15 | Lys Leu Lys Asp Gln Leu Asp Ile Asp Asp Asp Leu Lys Glu Tyr Asn 65 70 75 80 |
| 20 | Leu Glu Glu Tyr Asp Asp Glu Glu Ile Ala Asp Asn Glu Gly Gly Lys 85 90 95 |
| | Asp Val Ser Met Phe Pro Gly Leu Ser Asp Ser Asp Val Lys Phe 100 105 110 |
| 25 | His Glu Gly Glu Lys Gly Glu Asp Pro Tyr Ile Ser Leu Pro Asn Gln 115 120 125 |
| | Glu Asp Ser Gln Glu Glu Lys Gln Glu Leu Gln Val Tyr Pro Ser Asp 130 135 140 |
| 30 | Asn Leu Val Leu Ala Ala Arg Thr Glu Asp Asp Val Ser Tyr Leu Asp 145 150 155 160 |
| 35 | Ile Tyr Val Tyr Asp Asp Gly Ala Gly Phe His Ser Ser Asp Ile Pro 165 170 175 |
| | Val Glu Glu Gly Asp Glu Ala Asp Pro Asp Val Ala Arg Gly Leu Val 180 185 190 |
| 40 | Arg Asp Pro Ala Leu Tyr Val His His Asp Leu Met Leu Pro Ala Phe 195 200 205 |
| | Pro Leu Cys Val Glu Trp Leu Asp Tyr Lys Val Gly Ser Asn Ser Glu 210 215 220 |
| 45 | Glu Ala Ala Asn Tyr Ala Ala Ile Gly Thr Phe Asp Pro Gln Ile Glu 225 230 235 240 |

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| | - 142 |
|----|---|
| | Ile Trp Asn Leu Asp Cys Val Asp Lys Ala Phe Pro Asp Met Ile Leu 255 |
| 5 | Gly Glu Pro Leu Asp Asn Ser Met Val Ser Leu Lys Ser Lys Lys 260 265 270 |
| | Lys Lys Lys Ser Lys Thr Gly His Ile Thr Thr His His Thr Asp Ala 275 280 285 |
| 10 | Val Leu Ser Met Ala His Asn Lys Tyr Phe Arg Ser Val Leu Ala Ser 290 295 300 |
| | Thr Ser Ala Asp His Thr Val Lys Leu Trp Asp Leu Asn Ser Gly Asn 305 310 315 320 |
| 15 | Ala Ala Arg Ser Leu Ala Ser Ile His Ser Asn Lys Asn Val Ser Ser 325 330 335 |
| 20 | Ser Glu Trp His Met Leu Asn Gly Ser Ile Leu Leu Thr Gly Gly Tyr 340 345 350 |
| | Asp Ser Arg Val Ala Leu Thr Asp Val Arg Ile Ser Asp Glu Ser Gln 355 360 365 |
| 25 | Met Ser Lys Tyr Trp Ser Ala Met Ala Gly Glu Glu Ile Glu Thr Val 370 375 380 |
| | Thr Phe Ala Ser Glu Asn Ile Ile Leu Cys Gly Thr Asp Ser Gly Asn 395 400 |
| 30 | Val Tyr Ser Phe Asp Ile Arg Asn Asn Glu Asn Arg Lys Pro Val Trp 405 410 415 |
| 35 | Thr Leu Lys Ala His Asp Ala Gly Ile Ser Thr Leu Cys Ser Asn Lys 420 425 430 |
| | Phe Ile Pro Gly Met Met Ser Thr Gly Ala Met Gly Glu Lys Thr Val 435 440 445 |
| 40 | Lys Leu Trp Lys Phe Pro Leu Asp Asp Ala Thr Asn Thr Lys Gly Pro 450 455 460 |
| | Ser Met Val Leu Ser Arg Asp Phe Asp Val Gly Asn Val Leu Thr Ser 465 470 475 480 |
| 45 | Ser Phe Ala Pro Asp Ile Glu Val Ala Gly Thr Met Val Ile Gly Gly |

40

45

- 143 -485 490 495 Val Asn Lys Val Leu Lys Leu Trp Asp Val Phe Thr Asn Arg Ser Val 500 505 5 Arg Lys Ser Phe Lys Ser Glu Leu Glu Asn Val Gln Ala Arg Ala Lys 515 520 Glu Glu Ala Gln Lys Ile Gly Lys Ser Ser Arg Ile Ala Arg Lys Tyr 10 530 535 Thr Ser Asn Asp Asn Pro Asp Thr Val Ile Thr Ile Asp Asp Gln Gly 545 550 555 15 Glu Asp Glu Glu Glu Glu Gly Gly Asp Glu His Asp Asp Met Ala 565 570 575 (2) INFORMATION FOR SEQ ID NO:57: 20 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 325 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 25 (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO 30 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: PLAP, Fig. 40 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

Met His Tyr Met Ser Gly His Ser Asn Phe Val Ser Tyr Val Cys Ile

1 5

Ile Pro Ser Ser Asp Ile Tyr Pro His Gly Leu Ile Ala Thr Gly Gly 20

Asn Asp His Asn Ile Cys Ile Phe Ser Leu Asp Ser Pro Met Pro Leu 35 40 45

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| | - 144 - |
|----|--|
| | Tyr Ile Leu Lys Gly His Lys Asp Thr Val Cys Ser Leu Ser Ser Gly 50 55 60 |
| 5 | Lys Phe Gly Thr Leu Leu Ser Gly Ser Trp Asp Thr Thr Ala Lys Val 65 70 75 80 |
| | Trp Leu Asn Asp Lys Cys Met Met Thr Leu Gln Gly His Thr Ala Ala 85 90 95 |
| 10 | Val Trp Ala Val Lys Ile Leu Pro Glu Gln Gly Leu Met Leu Thr Gly 100 105 110 |
| _ | Ser Ala Asp Lys Thr Ile Lys Leu Trp Lys Ala Gly Arg Cys Glu Arg 115 120 125 |
| 15 | Thr Phe Leu Gly His Glu Asp Cys Val Arg Gly Leu Ala Ile Leu Ser 130 135 140 |
| 20 | Glu Thr Glu Phe Leu Ser Cys Ala Asn Asp Ala Ser Ile Arg Arg Trp 145 150 155 160 |
| | Gln Ile Thr Gly Glu Cys Leu Glu Val Tyr Phe Gly His Thr Asn Tyr 165 170 175 |
| 25 | Ile Tyr Ser Ile Ser Val Phe Pro Asn Ser Lys Asp Phe Val Thr Thr 180 185 190 |
| | Ala Glu Asp Arg Ser Leu Arg Ile Trp Lys His Gly Glu Cys Ala Gln 195 200 205 |
| 30 | Thr Ile Arg Leu Pro Ala Gln Ser Ile Trp Cys Cys Cys Val Leu Glu 210 215 220 |
| 35 | Asn Gly Asp Ile Val Val Gly Ala Ser Asp Gly Ile Ile Arg Val Phe 225 230 235 240 |
| | Thr Glu Ser Glu Glu Arg Thr Ala Ser Ala Glu Glu Ile Lys Ala Ser 245 250 255 |
| 40 | Leu Ser Arg Glu Ser Pro Leu Ile Ala Lys Val Leu Thr Thr Glu Pro 260 265 270 |
| | Pro Ile Ile Thr Pro Val Arg Arg Thr Leu Pro Cys Arg Val Thr Arg 275 280 285 |
| 45 | Ser Met Ile Ser Ser Cys Leu Ser Arg Leu Val Ser Thr Ser Leu Ser |

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290 295 300

Thr Ser Asp Ser His Leu Thr Ile Thr Ala Leu His Leu Phe Leu Thr 305 310 315 320

5

Thr Thr Thr Glu

325

(2) INFORMATION FOR SEQ ID NO:58:

10

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 425 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

15

- (ii) MOLECULE TYPE: protein
- (iii) HYPOTHETICAL: NO
- 20 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RETINOBLASTOMA BINDING PROTEIN -HUMAN, Fig. 41

25

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:
- Met Ala Asp Lys Glu Ala Ala Phe Asp Asp Ala Val Glu Glu Arg Val 30 5 15
 - Ile Asn Glu Glu Tyr Lys Ile Trp Lys Lys Asn Thr Pro Phe Leu Tyr 20 25
- Asp Leu Val Met Thr His Ala Leu Glu Trp Pro Ser Leu Thr Ala Gln 35 35 45
 - Trp Leu Pro Asp Val Thr Arg Pro Glu Gly Lys Asp Phe Ser Ile His 50 55 60

- Arg Leu Val Leu Gly Thr His Thr Ser Asp Glu Gln Asn His Leu Val 65 70 75
- Ile Ala Ser Val Gln Leu Pro Asn Asp Asp Ala Gln Phe Asp Ala Ser 45 85 90 95



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| | - 140 | | |
|----|--|---------------------------|----------------------------|
| | His Tyr Asp Ser Glu Lys Gly | Glu Phe Gly Gly Pi 105 | he Gly Ser Val Ser 110 |
| 5 | Gly Lys Ile Glu Ile Glu Ile 115 | Lys Ile Asn His G 120 | lu Gly Glu Val Asn 125 |
| | Arg Ala Arg Tyr Met Pro Gln 130 135 | | le Ala Thr Lys Thr .40 |
| 10 | Pro Ser Ser Asp Val Leu Val | Phe Asp Tyr Thr L | Lys His Pro Ser Lys 160 |
| | Pro Asp Pro Ser Gly Glu Cys | Asn Pro Asp Leu A 170 | Arg Leu Arg Gly His 175 |
| 15 | Gln Lys Glu Gly Tyr Gly Leu 180 | Ser Trp Asn Pro A | Asn Leu Ser Gly His 190 |
| 20 | Leu Leu Ser Ala Ser Asp Asp 195 | His Thr Ile Cys I | Leu Trp Asp Ile Ser 205 |
| | Ala Val Pro Lys Glu Gly Lys 210 215 | | Lys Thr Ile Phe Thr 220 |
| 25 | Gly His Thr Ala Val Val Glu 225 230 | Asp Val Ser Trp E | His Leu Leu His Glu 240 |
| | Ser Leu Phe Gly Ser Val Ala 245 | Asp Asp Gln Lys 1 250 | Leu Met Ile Trp Asp 255 |
| 30 | Thr Arg Ser Asn Asn Thr Ser 260 | Lys Pro Ser His : 265 | Ser Val Asp Ala His 270 |
| 35 | Thr Ala Glu Val Asn Cys Leu 275 | Ser Phe Asn Pro | Tyr Ser Glu Phe Ile 285 |
| | Leu Ala Thr Gly Ser Ala Asp 290 299 | | Leu Trp Asp Leu Arg 300 |
| 40 | Asn Leu Lys Leu Lys Leu His | s Ser Phe Glu Ser 315 | His Lys Asp Glu Ile 320 |
| | Phe Gln Val Gln Trp Ser Pr 325 | o His Asn Glu Thr 330 | Ile Leu Ala Ser Ser 335 |
| 45 | Gly Thr Asp Arg Arg Leu As | n Val Trp Asp Leu | Ser Lys Ile Gly Glu |

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340 345 350 Glu Gln Ser Pro Glu Asp Ala Glu Asp Gly Pro Pro Glu Leu Leu Phe 355 360 365 5 Ile His Gly Gly His Thr Ala Lys Ile Ser Asp Phe Ser Trp Asn Pro 370 375 Asn Glu Pro Trp Val Ile Cys Ser Val Ser Glu Asp Asn Ile Met Gln 10 385 390 395 Val Trp Gln Met Ala Glu Asn Ile Tyr Asn Asp Glu Asp Pro Glu Gly 405 410 15 Ser Val Asp Pro Glu Gly Gln Gly Ser 420 (2) INFORMATION FOR SEQ ID NO:59: 20 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 852 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 25 (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 30 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: S253 PROTEIN, Fig. 42 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:59: Met Phe Lys Ser Lys Thr Ser Thr Leu Ser Tyr Asp Glu Thr Pro Asn 5 40 Ser Asn Glu Gly Asp Arg Asn Ala Thr Pro Val Asn Pro Lys Glu Lys 25 Ser Gln Thr Lys His Leu Asn Ile Pro Gly Asp Arg Ser Arg His Ser 40 45 45

Ser Ile Ala Asp Ser Lys Arg Ser Ser Ser Arg Tyr Asp Gly Gly Tyr

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| | | | | | | - | | | | | | | | | | |
|----|------------|-------------|--------------|-------------|------------|------------|-------------|------------|------------|------------|------------|------------|--------------|------------|------------|------------|
| | | 50 | | | | | 55 | | | | | 60 | | | | |
| | Ser 65 | Ala | Asp | Ile | Ile | Pro 70 | Ala | Gln | Leu | Arg | Phe 75 | Ile | Asp | Asn | Ile | Asp 80 |
| 5 | Tyr | Gly | Thr | Arg | Leu 85 | Arg | Lys | Thr | Leu | His 90 | Arg | Asn | Ser | Val | Val 95 | Ser |
| 10 | Asn | Gly | Tyr | Asn 100 | Lys | Leu | Ser | Glu | Asn 105 | Asp | Arg | Trp | Tyr | Phe 110 | Asp | Leu |
| | Phe | Asp | Arg 115 | Lys | Tyr | Phe | Glu | Asn 120 | Tyr | Leu | Glu | Glu | Pro 125 | Thr | Tyr | Ile |
| 15 | Lys | Ile | Phe | Lys | Lys | Lys | Glu 135 | Gly | Leu | Glu | Gln | Phe 140 | Asp | Arg | Met | Phe |
| | Leu 145 | | Gln | Glu | Leu | Lys 150 | Ile | Pro | Asp | Val | Tyr 155 | Lys | Ser | Thr | Thr | Tyr 160 |
| 20 | Gl | Gly | , Glu | Pro | Ala 165 | Val | Ala | Asn | Ser | Glu 170 | Leu | Phe | Lys | Asn | Ser 175 | Ile |
| 25 | Cys | ; Суз | s Cys | Thr 180 | | Ser | His | Asp | Gly 185 | Lys | Tyr | Met | Val | Ile 190 | Gly | Cys |
| | Lys | s Ası | 9 Gly 195 | | Leu | His | Leu | Trp 200 | | Val | Ile | Asn | Ser 205 | Pro | Val | Lys |
| 30 | Arg | g Se: 21 | r Glu O | . Met | Gly | Arg | Ser 215 | | Lys | Ser | Val | Ser 220 | Ala | Ser | Arg | Ala |
| | As: | | r Lev | Lys | : Ile | Gln 230 | | His | Leu | Ala | Ser 235 | | . Ser | Ser | His | Asn 240 |
| 35 | Gl | y Se | r Ile | e Sei | Ser 245 | | a Asp | Leu | Lys | 250 | | : Asp | Glr. | Phe | 255 | Gly |
| 40 | Pr | o Se | r Ly: | s Gl: 26 | | ı His | s Lev | 1 Туі | 26! | | o Val | l Phe | e Tyr | 270 | | val |
| | Ph | le Ar | g Va 27 | | e Me | t Gli | u His | 28 | | u Asj | o Ile | e Le | u Ası 28! | | a Ası | n Trp |
| 45 | Se | | /s As 90 | n Gl | y Ph | e Le | u Ile 29 | | r Al | a Se | r Me | As 30 | | s Th | r Ala | a Lys |

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| | Leu 305 | | His | Pro | Glu | Arg | | Tyr | Ser | Leu | 1 Lys 315 | | Ph∈ | e Val | His | 320 |
|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|--------------|------------|------------|------------|--------------|------------|
| 5 | Asp | Phe | Val | Thr | Ser 325 | | Ile | Phe | Phe | 9rc 330 | | Asr |) Asp | Arg | 7 Phe 335 | e Ile |
| | Ile | Thr | Gly | Cys 340 | | Asp | His | Arg | Cys 345 | | Leu | Trp | Ser | Ile 350 | | Asp |
| 10 | Asn | Glu | Val 355 | Ser | Tyr | Ala | Phe | Asp 360 | | Lys | Asp | Leu | Ile 365 | Thr | Ser | Leu |
| 15 | Thr | Leu 370 | Ser | Pro | Pro | Gly | Gly 375 | Glu | Tyr | Thr | Ile | Ile 380 | Gly | Thr | Phe | Asn |
| | Gly 385 | Tyr | Ile | Tyr | Val | Leu 390 | Leu | Thr | His | Gly | Leu 395 | Lys | Phe | Val | Ser | Ser 400 |
| 20 | Phe | His | Val | Ser | Asp 405 | Lys | Ser | Thr | Gln | Gly 410 | Thr | Thr | Lys | Asn | Ser 415 | Phe |
| | His | Pro | Ser | Ser 420 | Glu | Tyr | Gly | Lys | Val 425 | Gln | His | Gly | Pro | Arg 430 | Ile | Thr |
| 25 | Gly | Leu | Gln 435 | Сув | Phe | Phe | Ser | Lys 440 | Val | Asp | Lys | Asn | Leu 445 | Arg | Leu | Ile |
| 30 | Val | Thr 450 | Thr | Asn | Asp | Ser | Lys 455 | Ile | Gln | Ile | Phe | Asp 460 | Leu | Asn | Glu | Lys |
| | 465 | | | | Leu | 470 | | | | | 475 | | | | | 480 |
| 35 | | | | | Leu 485 | | | | | 490 | | | | | 495 | |
| | | | | 500 | Trp | | | | 505 | | | | | 510 | | |
| 40 | | | 515 | | Asn | | | 520 | | | | | 525 | | | |
| 45 | | 530 | | | Leu | | 535 | | | | | 540 | | | - | |
| | Thr | Asn | Asp | Glu | Cys | Leu | Thr | Glu | Thr | Ser | Asn | Gln | Ser | Ser | Ser | His |

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| | | | | | | | 100 | | | | | | | | | |
|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|
| | 545 | | | | | 550 | | | | | 5 55 | | | | | 560 |
| - | Thr | Phe | Thr | Asn | Ser 565 | Ser | Lys | Asn | Val | Leu 570 | Gln | Thr | Gln | Thr | Val 575 | Gly |
| 5 | Ser | Gln | Ala | Ile 580 | Lys | Asn | Asn | His | Tyr 585 | Ile | Ser | Phe | His | Ala 590 | His | Asn |
| 10 | Ser | Pro | Val 595 | Thr | Cys | Ala | Ser | Ile 600 | Ala | Pro | Asp | Val | Ala 605 | Ile | Lys | Asn |
| | Leu | Ser 610 | Leu | Ser | Asn | Asp | Leu 615 | Ile | Phe | Glu | Leu | Thr 620 | Ser | Gln | Tyr | Phe |
| 15 | Lys 625 | Glu | Met | Gly | Gln | Asn 630 | Tyr | Ser | Glu | Ser | Lys 635 | Glu | Thr | Cys | Asp | Asn 640 |
| 20 | Lys | Pro | Asn | His | Pro 645 | Val | Thr | Glu | Thr | Gly 650 | Gly | Phe | Ser | Ser | Asn 655 | Leu |
| 20 | Ser | Asn | Val | Val 660 | Asn | Asn | Val | Gly | Thr 665 | Ile | Leu | Ile | Thr | Thr 670 | Asp | Ser |
| 25 | Gln | Gly | Leu 675 | Ile | Arg | Val | Phe | Arg 680 | Thr | Asp | Ile | Leu | Pro 685 | Glu | Ile | Arg |
| | Lys | Lys 690 | Ile | Ile | Glu | Lys | Phe 695 | His | Glu | Tyr | Asn | Leu 700 | Phe | His | Leu | Glu |
| 30 | Ala 705 | | Gly | Lys | Ile | Asn 710 | Asn | His | Asn | Asn | Asp 715 | Ser | Ile | Leu | Glu | Asn 720 |
| 35 | Arg | Met | Asp | Glu | Arg 725 | Ser | Ser | Thr | Glu | Asp 730 | Asn | Glu | Phe | Ser | Thr 735 | Thr |
| | Pro | Pro | Ser | Asn 740 | | His | Asn | Ser | Arg 745 | | Ser | His | Asp | Phe 750 | Cys | Glu |
| 40 | Leu | His | Pro 755 | Asn | Asn | Ser | Pro | Val 760 | Ile | Ser | Gly | Met | Pro 765 | Ser | Arg | Ala |
| | Ser | 770 | Ile | Phe | Lys | Asn | 775 | | Phe | Asn | Lys | Ser 780 | | Gly | Ser | Phe |
| 45 | Ile 785 | | Leu | Lys | Ser | 790 | | Glu | Ser | Thr | Ser 795 | | Thr | Val | Phe | Gly 800 |

- 151 -Pro His Asp Ile Pro Arg Val Ser Thr Thr Tyr Pro Lys Leu Lys Cys 805 810 815 Asp Val Cys Asn Gly Ser Asn Phe Glu Cys Ala Ser Lys Asn Pro Ile 5 820 825 830 Ala Gly Gly Asp Ser Gly Phe Thr Cys Ala Asp Cys Gly Thr Ile Leu 835 840 845 10 Asn Asn Phe Arg 850 (2) INFORMATION FOR SEQ ID NO:60: 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 488 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 20 (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO 25 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: SOF1, Fig. 43 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:60: 30 Met Lys Ile Lys Thr Ile Lys Arg Ser Ala Asp Asp Tyr Val Pro Val 5 10 15 Lys Ser Thr Gln Glu Ser Gln Met Pro Arg Asn Leu Asn Pro Glu Leu 35 20 25 30 His Pro Phe Glu Arg Ala Arg Glu Tyr Thr Lys Ala Leu Asn Ala Thr 35 40 40 Lys Leu Glu Arg Met Phe Ala Lys Pro Phe Val Gly Gln Leu Gly Tyr 50 Gly His Arg Asp Gly Val Tyr Ala Ile Ala Lys Asn Tyr Gly Ser Leu 45 65

70

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| | | | | | | | L52 | - | | | | | | | | |
|----|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | Asn | Lys | Leu | | Thr 85 | Gly : | Ser | Ala | Asp | Gly 90 | Val | Ile | Lys | Tyr | Trp 95 | Asn |
| 5 | Met | Ser | Thr | Arg 100 | Glu | Glu | Phe | | Ser 105 | Phe | Lys | Ala | His | Tyr 110 | Gly | Leu |
| | Val | Thr | Gly 115 | Leu | Cys | Val | Thr | Gln 120 | Pro | Arg | Phe | His | Asp 125 | Lys | Lys | Pro |
| 10 | Asp | Leu 130 | Lys | Ser | Gln | | Phe 135 | Met | Leu | Ser | Cys | Ser 140 | Asp | Asp | Lys | Thr |
| 15 | Val 145 | Lys | Leu | Trp | Ser | Ile 150 | Asn | Val | Asp | Asp | Tyr 155 | Ser | Asn | Lys | Asn | Ser 160 |
| 15 | Ser | Asp | Asn | Asp | Ser 165 | Val | Thr | Asn | Glu | Glu 170 | Gly | Leu | Ile | Arg | Thr 175 | Phe |
| 20 | Asp | Gly | Glu | Ser 180 | Ala | Phe | Gln | Gly | Ile 185 | Asp | Ser | His | Arg | Glu 190 | Asn | Ser |
| | Thr | Phe | Ala 195 | Thr | Gly | Gly | Ala | Lys 200 | Ile | His | Leu | Trp | Asp 205 | Val | Asn | Arg |
| 25 | Leu | Lys 210 | | Val | Ser | Asp | Leu 215 | Ser | Trp | Gly | Ala | Asp 220 | Asn | Ile | Thr | Ser |
| 20 | Leu 225 | | Phe | Asn | Gln | Asn 230 | Glu | Thr | Asp | Ile | Leu 235 | Ala | Ser | Thr | Gly | Ser 240 |
| 30 | Asp | Asn | Ser | Ile | Val 245 | Leu | Tyr | Asp | Leu | Arg 250 | Thr | Asn | Ser | Pro | Thr 255 | Gln |
| 35 | Lys | Ile | val | Gln 260 | | Met | Arg | Thr | Asn 265 | Ala | Ile | Cys | Trp | Asn 270 | | Met |
| | Glu | Ala | 275 | | Phe | Val | Thr | Ala 280 | | Glu | Asp | His | Asn 285 | | Tyr | Tyr |
| 40 | Tyr | 290 | | . Arg | Asn | Leu | Ser 295 | | Ser | : Leu | . Asn | Val 300 | | Lys | Asp | His |
| 45 | Val | | r Ala | ı Val | . Met | 310 | | . Asp | Phe | e Ser | 315 | | Gly | Asp | Glu | 320 |
| 45 | Val | l Th | r Gly | , Sei | т Туз | : Asp | Lys | s Ser | : Ile | e Arg | ; Ile | туг | Lys | Thi | : Ası | n His |

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Gly His Ser Arg Glu Ile Tyr His Thr Lys Arg Met Gln His Val Phe Val Lys Tyr Ser Met Asp Ser Lys Tyr Ile Ile Ser Gly Ser Asp Asp Gly Asn Val Arg Leu Trp Arg Ser Lys Ala Trp Glu Arg Ser Asn Val Lys Thr Thr Arg Glu Lys Asn Lys Leu Glu Tyr Asp Glu Lys Leu Lys Glu Arg Phe Arg His Met Pro Glu Ile Lys Arg Ile Ser Arg His Arg His Val Pro Gln Val Ile Lys Lys Ala Gln Glu Ile Lys Asn Ile Glu Leu Ser Ser Ile Lys Arg Arg Glu Ala Asn Glu Arg Arg Thr Arg Lys Asp Met Pro Tyr Ile Ser Glu Arg Lys Lys Gln Ile Val Gly Thr Val His Lys Tyr Glu Asp Ser Gly Arg Asp Arg Lys Arg Lys Glu Asp Asp Lys Arg Asp Thr Gln Glu Lys (2) INFORMATION FOR SEQ ID NO:61: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 423 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

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(C) INDIVIDUAL ISOLATE: STE4 - YEAST, Fig. 44

| | (xi) | SEQU | ENCE | DES | CRIP? | rion | : SE(|) ID | NO: | 61: | | | | | | |
|----|-----------|-----------|-----------|-----------|------------|-----------|------------|-----------|-----------|-----------|-----------|------------|-----------|-----------|-----------|-----------|
| 5 | Met 1 | Ala | Ala : | | Gln 1 5 | Met i | Asp S | Ser | Ile | Thr 10 | Tyr | Ser | Asn . | Asn | Val 15 | Thr |
| 10 | Gln | Gln | Tyr | Ile 20 | Gln | Pro | Gln : | | Leu 25 | Gln | Asp | Ile | Ser | Ala 30 | Val | Glu |
| | Asp | Glu | Ile 35 | Gln | Asn | Lys | | Glu 40 | Ala | Ala | Arg | Gln | Glu 45 | Ser | Lys | Gln |
| 15 | Leu | His 50 | Ala | Gln | Ile | Asn | Lys 55 | Ala | Lys | His | Lys | Ile 60 | Gln | Asp | Ala | Ser |
| | Leu 65 | Phe | Gln | Met | Ala | Asn 70 | Lys | Val | Thr | Ser | Leu 75 | Thr | Lys | Asn | Lys | Ile 80 |
| 20 | Asn | Leu | Lys | Pro | Asn 85 | Ile | Val | Leu | Lys | Gly 90 | His | Asn | Asn | Lys | Ile 95 | Ser |
| 25 | | | Arg | 100 | | | | | 105 | | | | | 110 | | |
| | | | 115 | | | | | 120 | | | | | 125 | | | Asn |
| 30 | | 130 |) | | | | 135 | | | | | 140 | | | | Pro |
| 25 | 14 | 5 | | | | 150 |) | | | | 155 | • | | | | 160 |
| 35 | | | | | 169 | 5 | | | | 17 | 0 | | | | 17 | |
| 40 | | | | 18 | 0 | | | | 18 | 5 | | | | 19 | U | p Asn |
| | | | 19 | 5 | | | | 20 | 0 | | | | 20 | 5 | | p Asp |
| 45 | 13 | | co Ly | s Al | a Ly | s Ar | g Va 21 | | g Gl | .и Ту | r Se | r As 22 | p Hi O | s Le | u Gl | y Asp |

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Val Leu Ala Leu Ala Ile Pro Glu Glu Pro Asn Leu Glu Asn Ser Ser Asn Thr Phe Ala Ser Cys Gly Ser Asp Gly Tyr Thr Tyr Ile Trp Asp Ser Arg Ser Pro Ser Ala Val Gln Ser Phe Tyr Val Asn Asp Ser Asp Ile Asn Ala Leu Arg Phe Phe Lys Asp Gly Met Ser Ile Val Ala Gly Ser Asp Asn Gly Ala Ile Asn Met Tyr Asp Leu Arg Ser Asp Cys Ser Ile Ala Thr Phe Ser Leu Phe Arg Gly Tyr Glu Glu Arg Thr Pro Thr Pro Thr Tyr Met Ala Ala Asn Met Glu Tyr Asn Thr Ala Gln Ser Pro Gln Thr Leu Lys Ser Thr Ser Ser Ser Tyr Leu Asp Asn Gln Gly Val Val Ser Leu Asp Phe Ser Ala Ser Gly Arg Leu Met Tyr Ser Cys Tyr Thr Asp Ile Gly Cys Val Val Trp Asp Val Leu Lys Gly Glu Ile Val Gly Lys Leu Glu Gly His Gly Gly Arg Val Thr Gly Val Arg Ser Ser Pro Asp Gly Leu Ala Val Cys Thr Gly Ser Trp Asp Ser Thr Met Lys Ile Trp Ser Pro Gly Tyr Gln

(2) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 704 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

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| | (ii) ! | MOLE | CULE | TYP | E: pi | rote | in | | | | | | | | | |
|----|------------|-------------|-------------|-------------|-------------|-----------|------------|------------|------------|-----------|------------|------------|------------|------------|------------|-----------|
| | (iii) | HYPO' | THET | ICAL | : NO | | | | | | | | | | | |
| 5 | (iv) | ANTI | -SEN | SE: | NO | | | | | | | | | | | |
| | (vi) | ORIG (C) | LANI ONI | SOU IVID | RCE: UAL | ISOL | ATE: | TRA | NSCR | IPTI | ON F | acto | R TI | IF, | Fig. | 45 |
| 10 | (xi) | SEQU | ENCE | DES | CRIP | TION | : SE | Q ID | NO: | 62: | | | | | | |
| | Met 1 | Ser | Leu | Glu | Val 5 | Ser | Asn | Ile | Asn | Gly 10 | Gly | Asn | Gly | Thr | Gln 15 | Leu |
| 15 | Ser | His | Asp | Lys 20 | Arg | Glu | Leu | Leu | Cys 25 | Leu | Leu | Lys | Leu | Ile 30 | Lys | Lys |
| 20 | Tyr | Gln | Leu 35 | Lys | Ser | Thr | Glu | Glu 40 | Leu | Leu | Cys | Gln | Glu 45 | Ala | Asn | Val |
| | Ser | Ser 50 | Val | Glu | Leu | Ser | Glu 55 | Ile | Ser | Glu | Ser | Asp 60 | Val | Gln | Gln | Val |
| 25 | Leu 65 | Gly | Ala | Val | Leu | Gly 70 | Ala | Gly | Asp | Ala | Asn 75 | Arg | Glu | Arg | Lys | His 80 |
| | Val | Gln | Ser | Pro | Ala 85 | Gln | Gly | His | Lys | Gln 90 | Ser | Ala | Val | Thr | Glu 95 | Ala |
| 30 | Asn | Ala | Ala | Glu 100 | | Leu | Ala | Lys | Phe 105 | Ile | Asp | Asp | Asp | Ser 110 | Phe | Asp |
| 35 | Ala | Gln | His | | Glu | Gln | Ala | Tyr 120 | | Glu | Leu | Arg | Thr 125 | Phe | Val | Glu |
| | Asp | Ser 130 | | Asp | Ile | Tyr | Lys 135 | | Glu | Leu | Ser | Met 140 | | Leu | Tyr | Pro |
| 40 | Ile 145 | | val | Glr | l Ile | 150 | | Lys | : Ile | e Leu | Ala 155 | | Gly | Leu | Arg | Gli 16 |
| | Lys | s Ala | a Lys | ; Glu | Phe | | e Glu | Lys | з Туг | 170 | | Asp | Leu | Asp | Gly 175 | |

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| | Ту | r Il | e Gl | u Gl 18 | | u Ph | e As | n Le | u Le 18 | | eu Le | eu Se | er Ly | | ro G 90 | lu Glu |
|----|--------------|------------|--------------|------------|------------|------------|------------|------------|-------------------|------------|------------|------------|------------|------------|------------|---------------|
| 5 | Lei | ı Le | u Gli 199 | ı As: | n As | p Le | u Va | l Va 20 | | a Me | et Gl | u Gl | n As | | ys Pl | ne Val |
| | Ile | 21 | g Met | : Se: | r Arg | g Asl | 215 | | s Se | r Le | u Ph | e Ly 22 | | g Hi | s Il | le Gln |
| 10 | Asp 225 | Arg | J Arg | Glr | n Glu | ı Val | | . Ala | a As _l | o Il | e Va: | | r Ly | s Ty | r Le | eu His 240 |
| 15 | Phe | Asp | Thr | Туг | Glu 245 | | Met | Ala | a Arg | 250 | | 5 Let | ı Gl | n Cy | s Va 25 | l Ala 5 |
| | Thr | Ala | Gly | Ser 260 | | Leu | Gly | Glu | 265 | | s Arg | g Glr | ı Ası | 27 | | s Met |
| 20 | Arg | Val | Tyr 275 | Tyr | Gly | Leu | Leu | Lys 280 | | Val | . Asp | Phe | Glr 285 | | r Let | 1 Thr |
| | Thr | Pro 290 | Ala | Pro | Ala | Pro | Glu 295 | Glu | Glu | Asp | Asp | Asp 300 | Pro | Asp | Ala | a Pro |
| 25 | Asp 305 | Arg | Pro | Lys | Lys | Lys 310 | Lys | Pro | Lys | Lys | Asp 315 | Pro | Leu | Leu | . Ser | Lys 320 |
| 30 | Lys | Ser | Lys | Ser | Asp 325 | Pro | Asn | Ala | Pro | Ser 330 | Ile | Asp | Arg | Ile | Pro | Leu |
| | Pro | Glu | Leu | Lys 340 | Asp | Ser | Asp | Lys | Leu 345 | Leu | Lys | Leu | Lys | Ala 350 | Leu | Arg |
| 35 | | | Ser 355 | | | | | 360 | | | | | 365 | | | |
| | Val | Phe 370 | Tyr | Thr | Val | | Asn 375 | Ser | His | Gln | Gly | Val 380 | Thr | Cys | Ala | Glu |
| 40 | Ile : 385 | | | | | 390 | | | | | 395 | | | | | 400 |
| 45 | Val 2 | | | | 405 | | | | | 410 | | | | | 415 | |
| | Ala 1 | Asp | Ser 1 | Leu . | Arg | Glu | Leu i | Asp | Lys | Glu | Ser | Ala | Asp | Ile | Asn | Val |

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| | | | 130 | |
|------------|--------------------|---------------------|----------------------------------|------------------------------|
| | | 420 | 425 | 430 |
| | Arg Met Leu | Asp Asp Arg | g Ser Gly Glu Val Thr 440 | Arg Ser Leu Met Gly 445 |
| 5 | His Thr Gly | Pro Val Tyr | r Arg Cys Ala Phe Ala 455 | Pro Glu Met Asn Leu 460 |
| 10 | Leu Leu Ser 465 | Cys Ser Gli 470 | u Asp Ser Thr Ile Arg 0 475 | Leu Trp Ser Leu Leu 480 |
| | Thr Trp Ser | Cys Val Val | l Thr Tyr Arg Gly His 490 | Val Tyr Pro Val Trp 495 |
| 15 | Asp Val Arg | Phe Ala Pro | o His Gly Tyr Tyr Phe 505 | Val Ser Cys Ser Tyr 510 |
| | Asp Lys Thi | | eu Trp Ala Thr Asp Ser 520 | Asn Gln Ala Leu Arg 525 |
| 20 | Val Phe Val | Gly His Le | eu Ser Asp Val Asp Cys 535 | Val Gln Phe His Pro 540 |
| 25 | Asn Ser Ası 545 | n Tyr Val Al 55 | la Thr Gly Ser Ser Asp 50 555 | |
| | Trp Asp As | n Met Thr Gl 565 | ly Gln Ser Val Arg Leu 570 | Met Thr Gly His Lys 575 |
| 3 <u>0</u> | Gly Ser Va | l Ser Ser Le 580 | eu Ala Phe Ser Ala Cys 585 | Gly Arg Tyr Leu Ala 590 |
| 25 | Ser Gly Se | | is Asn Ile Ile Ile Trp 600 | Asp Leu Ser Asn Gly 605 |
| 35 | Ser Leu Va 610 | l Thr Thr Le | eu Leu Arg His Thr Ser 615 | Thr Val Thr Thr Ile |
| 40 | Thr Phe Se | | ly Thr Val Leu Ala Ala 30 63 | |
| | Asn Leu Th | r Leu Trp A: 645 | sp Phe His Lys Val Th | r Glu Asp Tyr Ile Ser 655 |
| 45 | Asn His I | e Thr Val S | Ser His His Gln Asp Gl 665 | u Asn Asp Glu Asp Val 670 |

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Tyr Leu Met Arg Thr Phe Pro Ser Lys Asn Ser Pro Phe Val Ser Leu 675 680 685

His Phe Thr Arg Arg Asn Leu Leu Met Cys Val Gly Leu Phe Lys Ser 690 695 700

(2) INFORMATION FOR SEQ ID NO:63:

- 10 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 713 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 15 (ii) MOLECULE TYPE: protein
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
- 20

35

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: TUP1, Fig. 46
- 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

Met Thr Ala Ser Val Ser Asn Thr Gln Asn Lys Leu Asn Glu Leu Leu 1 5 10 15

- Asp Ala Ile Arg Gln Glu Phe Leu Gln Val Ser Gln Glu Ala Asn Thr 20 25 30
 - Tyr Arg Leu Gln Asn Gln Lys Asp Tyr Asp Phe Lys Met Asn Gln Gln
 35 40 45
 - Leu Ala Glu Met Gln Gln Ile Arg Asn Thr Val Tyr Glu Leu Glu Leu 50 55 60
- Thr His Arg Lys Met Lys Asp Ala Tyr Glu Ala Glu Ile Lys His Leu
 40 65 70 75 80
 - Lys Leu Gly Leu Glu Gln Arg Asp His Gln Ile Ala Ser Leu Thr Val 85 90 95

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| | - 160 |
|-------|---|
| | Gln Gln Gln Gln Gln Leu Ala Ala Ala Ser Ala Ser Val Pro Val 115 120 125 |
| 5 | Ala Gln Gln Pro Pro Ala Thr Thr Ser Ala Thr Ala Thr Pro Ala Ala 130 135 140 |
| | Asn Thr Thr Gly Ser Pro Ser Ala Phe Pro Val Gln Ala Ser Arg 145 150 155 160 |
| 10 | Pro Asn Leu Val Gly Ser Gln Leu Pro Thr Thr Leu Pro Val Val 165 170 175 |
| | Ser Ser Asn Ala Gln Gln Gln Leu Pro Gln Gln Gln Leu Gln Gln Gln 180 185 190 |
| 15 | Gln Leu Gln Gln Gln Pro Pro Pro Gln Val Ser Val Ala Pro Leu 195 200 205 |
| 20 | Ser Asn Thr Ala Ile Asn Gly Ser Pro Thr Ser Lys Glu Thr Thr 210 215 220 |
| | Leu Pro Ser Val Lys Ala Pro Glu Ser Thr Leu Lys Glu Thr Glu Pro 225 230 235 240 |
| 25 | Glu Asn Asn Asn Thr Ser Lys Ile Asn Asp Thr Gly Ser Ala Thr Thr 245 250 255 |
| | Ala Thr Thr Thr Ala Thr Glu Thr Glu Ile Lys Pro Lys Glu Glu 260 265 270 |
| 3.0 - | Asp Ala Thr Pro Ala Ser Leu His Gln Asp His Tyr Leu Val Pro Tyr 275 280 285 |
| 35 | Asn Gln Arg Ala Asn His Ser Lys Pro Ile Pro Pro Phe Leu Leu Asp 290 295 300 |
| | Leu Asp Ser Gln Ser Val Pro Asp Ala Leu Lys Lys Gln Thr Asn Asp 305 310 315 320 |
| 40 | Tyr Tyr Ile Leu Tyr Asn Pro Ala Leu Pro Arg Glu Ile Asp Val Glu 325 330 335 |
| | Leu His Lys Ser Leu Asp His Thr Ser Val Val Cys Cys Val Lys Phe 340 345 350 |
| 45 | Ser Asn Asp Gly Glu Tyr Leu Ala Thr Gly Cys Asn Lys Thr Thr Gln |

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Val Tyr Arg Val Ser Asp Gly Ser Leu Val Ala Arg Leu Ser Asp Asp Ser Ala Ala Asn Asn His Arg Asn Ser Ile Thr Glu Asn Asn Thr Thr Thr Ser Thr Asp Asn Asn Thr Met Thr Thr Thr Thr Thr Thr Thr Ile Thr Thr Thr Ala Met Thr Ser Ala Ala Glu Leu Ala Lys Asp Val Glu Asn Leu Asn Thr Ser Ser Ser Pro Ser Ser Asp Leu Tyr Ile Arg Ser Val Cys Phe Ser Pro Asp Gly Lys Phe Leu Ala Thr Gly Ala Glu Asp Arg Leu Ile Arg Ile Trp Asp Ile Glu Asn Arg Lys Ile Val Met Ile Leu Gln Gly His Glu Gln Asp Ile Tyr Ser Leu Asp Tyr Phe Pro Ser Gly Asp Lys Leu Val Ser Gly Ser Gly Asp Arg Thr Val Arg Ile Trp Asp Leu Arg Thr Gly Gln Cys Ser Leu Thr Leu Ser Ile Glu Asp Gly Val Thr Thr Val Ala Val Ser Pro Gly Asp Gly Lys Tyr Ile Ala Ala Gly Ser Leu Asp Arg Ala Val Arg Val Trp Asp Ser Glu Thr Gly Phe Leu Val Glu Arg Leu Asp Ser Glu Asn Glu Ser Gly Thr Gly His Lys Asp Ser Val Tyr Ser Val Val Phe Thr Arg Asp Gly Gln Ser Val Val Ser Gly Ser Leu Asp Arg Ser Val Lys Leu Trp Asn Leu Gln Asn Ala

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|----|--|
| | Asn Asn Lys Ser Asp Ser Lys Thr Pro Asn Ser Gly Thr Cys Glu Val 610 615 620 |
| 5 | Thr Tyr Ile Gly His Lys Asp Phe Val Leu Ser Val Ala Thr Thr Gln 625 630 635 640 |
| | Asn Asp Glu Tyr Ile Leu Ser Gly Ser Lys Asp Arg Gly Val Leu Phe 645 650 655 |
| 10 | Trp Asp Lys Lys Ser Gly Asn Pro Leu Leu Met Leu Gln Gly His Arg 660 665 670 |
| - | Asn Ser Val Ile Ser Val Ala Val Ala Asn Gly Ser Ser Leu Gly Pro 675 680 685 |
| 15 | Glu Tyr Asn Val Phe Ala Thr Gly Ser Gly Asp Cys Lys Ala Arg Ile 690 695 700 |
| 20 | Trp Lys Tyr Lys Lys Ile Ala Pro Asn 705 710 |
| | (2) INFORMATION FOR SEQ ID NO:64: |
| 25 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 798 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| 30 | (ii) MOLECULE TYPE: protein |
| | (iii) HYPOTHETICAL: NO |
| | (iv) ANTI-SENSE: NO |
| 35 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG, Fig. 47</pre> |
| 40 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:64: |
| | Met Ser Gln Lys Gln Ser Thr Asn Gln Asn Gln Asn Gly Thr His Gln 1 5 10 15 |
| 45 | Pro Gln Pro Val Lys Asn Gln Arg Thr Asn Asn Ala Ala Gly Ala Asn 20 25 30 |

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| | Ser Gly Gln Gln Pro Gln Gln Gln Ser Gln Gly Gln Ser Gln Gln Gln 35 40 45 |
|----|---|
| 5 | Gly Arg Ser Asn Gly Pro Phe Ser Ala Ser Asp Leu Asn Arg Ile Val 50 55 60 |
| | Leu Glu Tyr Leu Asn Lys Lys Gly Tyr His Arg Thr Glu Ala Met Leu 65 70 75 80 |
| 10 | Arg Ala Glu Ser Gly Arg Thr Leu Thr Pro Gln Asn Lys Gln Ser Pro 85 90 95 |
| 15 | Ala Asn Thr Lys Thr Gly Lys Phe Pro Glu Gln Ser Ser Ile Pro Pro 100 105 110 |
| | Asn Pro Gly Lys Thr Ala Lys Pro Ile Ser Asn Pro Thr Asn Leu Ser 115 120 125 |
| 20 | Ser Lys Arg Asp Ala Glu Gly Gly Ile Val Ser Ser Gly Arg Leu Glu 130 135 140 |
| 25 | Gly Leu Asn Ala Pro Glu Asn Tyr Ile Arg Ala Tyr Ser Met Leu Lys 145 150 155 160 |
| 25 | Asn Trp Val Asp Ser Ser Leu Glu Ile Tyr Lys Pro Glu Leu Ser Tyr 165 170 175 |
| 30 | Ile Met Tyr Pro Ile Phe Ile Tyr Leu Phe Leu Asn Leu Val Ala Lys 180 185 190 |
| | Asn Pro Val Tyr Ala Arg Arg Phe Phe Asp Arg Phe Ser Pro Asp Phe 195 200 205 |
| 35 | Lys Asp Phe His Gly Ser Glu Ile Asn Arg Leu Phe Ser Val Asn Ser 210 220 Ile Asp His Ile Lys Cly Asp Cl |
| 40 | Ile Asp His Ile Lys Glu Asn Glu Val Ala Ser Ala Phe Gln Ser His 225 230 235 240 Lys Tyr Arg Ile Thr Met Ser Lys The Th |
| | Lys Tyr Arg Ile Thr Met Ser Lys Thr Thr Leu Asn Leu Leu Tyr 245 250 255 Phe Leu Asn Glu Asn Glu Ser Ile Glu Ser |
| 45 | Phe Leu Asn Glu Asn Glu Ser Ile Gly Gly Ser Leu Ile Ile Ser Val 260 265 270 |
| | Ile Asn Gln His Leu Asp Pro Asn Ile Val Glu Ser Val Thr Ala Arg |

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| | - 164 - | |
|----|---|--|
| | 275 280 285 | |
| | Glu Lys Leu Ala Asp Gly Ile Lys Val Leu Ser Asp Ser Glu Asn Gly 290 295 300 | |
| 5 | Asn Gly Lys Gln Asn Leu Glu Met Asn Ser Val Pro Val Lys Leu Gly 305 310 315 320 | |
| 10 | Pro Phe Pro Lys Asp Glu Glu Phe Val Lys Glu Ile Glu Thr Glu Leu 325 330 335 | |
| | Lys Ile Lys Asp Asp Gln Glu Lys Gln Leu Asn Gln Gln Thr Ala Gly 340 345 350 | |
| 15 | Asp Asn Tyr Ser Gly Ala Asn Asn Arg Thr Leu Leu Gln Glu Tyr Lys 355 360 365 | |
| | Ala Met Asn Asn Glu Lys Phe Lys Asp Asn Thr Gly Asp Asp Asp Lys 370 375 380 | |
| 20 | Asp Lys Ile Lys Asp Lys Ile Ala Lys Asp Glu Glu Lys Lys Glu Ser 385 390 395 400 | |
| 25 | Glu Leu Lys Val Asp Gly Glu Lys Lys Asp Ser Asn Leu Ser Ser Pro 405 410 415 | |
| | Ala Arg Asp Ile Leu Pro Leu Pro Pro Lys Thr Ala Leu Asp Leu Lys 420 425 430 | |
| 30 | Leu Glu Ile Gln Lys Val Lys Glu Ser Arg Asp Ala Ile Lys Leu Asp 435 440 445 | |
| | Asn Leu Gln Leu Ala Leu Pro Ser Val Cys Met Tyr Thr Phe Gln Asn 450 455 460 | |
| 35 | Thr Asn Lys Asp Met Ser Cys Leu Asp Phe Ser Asp Asp Cys Arg Ile 465 470 475 480 | |
| 40 | Ala Ala Ala Gly Phe Gln Asp Ser Tyr Ile Lys Ile Trp Ser Leu Asp 485 490 495 | |
| | Gly Ser Ser Leu Asn Asn Pro Asn Ile Ala Leu Asn Asn Asn Asp Lys 500 505 510 | |
| 45 | Asp Glu Asp Pro Thr Cys Lys Thr Leu Val Gly His Ser Gly Thr Val 515 520 525 | |

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| | Tyr Ser Thr Ser Phe Ser Pro Asp Asn Lys Tyr Leu Leu Ser Gly Ser 530 540 |
|-----|---|
| 5 | Glu Asp Lys Thr Val Arg Leu Trp Ser Met Asp Thr His Thr Ala Leu 545 550 555 560 |
| | Val Ser Tyr Lys Gly His Asn His Pro Val Trp Asp Val Ser Phe Ser 565 570 575 |
| 10 | Pro Leu Gly His Tyr Phe Ala Thr Ala Ser His Asp Gln Thr Ala Arg 580 585 590 |
| 15 | Leu Trp Ser Cys Asp His Ile Tyr Pro Leu Arg Ile Phe Ala Gly His 595 600 605 |
| | Leu Asn Asp Val Asp Cys Val Ser Phe His Pro Asn Gly Cys Tyr Val 610 615 620 |
| 20 | Phe Thr Gly Ser Ser Asp Lys Thr Cys Arg Met Trp Asp Val Ser Thr 625 630 635 640 |
| 0.5 | Gly Asp Ser Val Arg Leu Phe Leu Gly His Thr Ala Pro Val Ile Ser 645 650 655 |
| 25 | Ile Ala Val Cys Pro Asp Gly Arg Trp Leu Ser Thr Gly Ser Glu Asp 660 665 670 |
| 30 | Gly Ile Ile Asn Val Trp Asp Ile Gly Thr Gly Lys Arg Leu Lys Gln 675 680 685 |
| | Met Arg Gly His Gly Lys Asn Ala Ile Tyr Ser Leu Ser Tyr Ser Lys 690 695 700 |
| 35 | Glu Gly Asn Val Leu Ile Ser Gly Gly Ala Asp His Thr Val Arg Val 705 710 715 720 |
| 40 | Trp Asp Leu Lys Lys Ala Thr Thr Glu Pro Ser Ala Glu Pro Asp Glu 725 730 735 |
| | Pro Phe Ile Gly Tyr Leu Gly Asp Val Thr Ala Ser Ile Asn Gln Asp 740 745 750 |
| 45 | Ile Lys Glu Tyr Gly Arg Arg Thr Val Ile Pro Thr Ser Asp Leu 755 760 765 |
| | Val Ala Ser Phe Tyr Thr Lys Lys Thr Pro Val Phe Lys Val Lys Phe |

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770 775 780

Ser Arg Ser Asn Leu Ala Leu Ala Gly Gly Ala Phe Arg Pro 785 790 795

- (2) INFORMATION FOR SEQ ID NO:65:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 439 amino acids
- 10 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: protein
- 15. (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 20 (C) INDIVIDUAL ISOLATE: YCU7, Fig. 48
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:
- Met Val Arg Arg Phe Arg Gly Lys Glu Leu Ala Ala Thr Thr Phe Asn

 1 5 10 15
 - Gly His Arg Asp Tyr Val Met Gly Ala Phe Phe Ser His Asp Gln Glu 20 25 30
- Lys Ile Tyr Thr Val Ser Lys Asp Gly Ala Val Phe Val Trp Glu Phe
 35 40 45
- Thr Lys Arg Pro Ser Asp Asp Asp Asp Asp Glu Ser Glu Asp Asp Asp Asp 35 50 55 60
 - Lys Gln Glu Glu Val Asp Ile Ser Lys Tyr Ser Trp Arg Ile Thr Lys 65 70 75 80
- Lys His Phe Phe Tyr Ala Asn Gln Ala Lys Val Lys Cys Val Thr Phe 85 90 95
 - His Pro Ala Thr Arg Leu Leu Ala Val Gly Phe Thr Ser Gly Glu Phe
 100 105 110
- 45 Arg Leu Tyr Asp Leu Pro Asp Phe Thr Leu Ile Gln Gln Leu Ser Met

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Gly Gln Asn Pro Val Asn Thr Val Ser Val Asn Gln Thr Gly Glu Trp Leu Ala Phe Gly Ser Ser Lys Leu Gly Gln Leu Leu Val Tyr Glu Trp Gln Ser Glu Ser Tyr Ile Leu Lys Gln Gln Gly His Phe Asp Ser Thr Asn Ser Leu Ala Tyr Ser Pro Asp Gly Ser Arg Val Val Thr Ala Ser Glu Asp Gly Lys Ile Lys Val Trp Asp Ile Thr Ser Gly Phe Cys Leu Ala Thr Phe Glu Glu His Thr Ser Ser Val Thr Ala Val Gln Phe Ala Lys Arg Gly Gln Val Met Phe Ser Ser Leu Asp Gly Thr Val Arg Ala Trp Asp Leu Ile Arg Tyr Arg Asn Phe Arg Thr Phe Thr Gly Thr Glu Arg Ile Gln Phe Asn Cys Leu Ala Val Asp Pro Ser Gly Glu Val Val Cys Ala Gly Ser Leu Asp Asn Phe Asp Ile His Val Trp Ser Val Gln Thr Gly Gln Leu Leu Asp Ala Leu Ser Gly His Glu Gly Pro Val Ser Cys Leu Ser Phe Ser Gln Glu Asn Ser Val Leu Ala Ser Ala Ser Trp Asp Lys Thr Ile Arg Ile Trp Ser Ile Phe Gly Arg Ser Gln Gln Val Glu Pro Ile Glu Val Tyr Ser Asp Val Leu Ala Leu Ser Met Arg

Pro Asp Gly Lys Glu Val Ala Val Ser Thr Leu Lys Gly Gln Ile Ser

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Ile Phe Asn Ile Glu Asp Ala Lys Gln Val Gly Asn Ile Asp Cys Arg 380 375 370 Lys Asp Ile Ile Ser Gly Arg Phe Asn Gln Asp Arg Phe Thr Ala Lys 395 390 385 5 Ile Leu Asn Asp Pro Asn Phe Leu Leu Gln Tyr Ile Thr Val Leu Met 410 405 Val Trp Leu Leu Trp Leu Val Val Ile Ile Thr Pro Phe Val Tyr Met 10 430 425 420 Met Phe Gln Met Lys Ser Cys 435 15 (2) INFORMATION FOR SEQ ID NO:66: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 514 amino acids (B) TYPE: amino acid 20 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: protein (iii) HYPOTHETICAL: NO 25 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN, Fig. 49 30 ----(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66: Met Ser Thr Leu Ile Pro Pro Pro Ser Lys Lys Gln Lys Lys Glu Ala 35 15 5 Gln Leu Pro Arg Glu Val Ala Ile Ile Pro Lys Asp Leu Pro Asn Val 30 20 40 Ser Ile Lys Phe Gln Ala Leu Asp Thr Gly Asp Asn Val Gly Gly Ala 45 40 Leu Arg Val Pro Gly Ala Ile Ser Glu Lys Gln Leu Glu Glu Leu Leu 60 55 50 45

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| | As: | n Gl | n Le | u As | n Gly | 7 Thi | r Sei | r As | p Ası | o Pr | o Va 75 | l Pr | о ту | r Th | ır Pl | ne Ser 80 |
|----|------------|--------------|--------------|------------|-------------|------------|------------|------------|------------|-------------|------------|------------|--------------|------------|------------|--------------|
| 5 | Cys | s T h | r Ile | e Gl: | n Gly 85 | / Lys | s Lys | s Ala | a Sei | 2 Ası 90 | p Pro | o Va | l Ly | s Th | r Il 95 | e Asp |
| | Ile | ∋ Th | r Ası | 100 | | ı Tyr | Ser | Sei | Leu 105 | | ⊇ Lys | s Pro | o Gl | y Ty 11 | | n Ser |
| 10 | Thr | Gl: | u Asp 115 | | n Ile | Thr | Leu | Leu 120 | | Thr | Pro | Arg | y Ala 125 | | l Ph | e Lys |
| 15 | Val | . Lys | s Pro | Val | L Thr | Arg | Ser | Ser | Ser | Ala | Ile | Ala | | 7 His | s Gl | y Ser |
| 15 | Thr 145 | · Ile | e Leu | Cys | s Ser | Ala 150 | Phe | Ala | Pro | His | Thr | | Ser | Arg | g Met | Val 160 |
| 20 | Thr | Gly | ⁄ Ala | Gly | Asp | Asn | Thr | Ala | Arg | Ile 170 | Trp | Asp | Cys | Asp | Thr 175 | Gln |
| | Thr | Pro | Met | His 180 | Thr | Leu | Lys | Gly | His 185 | Tyr | Asn | Trp | Val | Leu 190 | | Val |
| 25 | Ser | Trp | Ser 195 | Pro | Asp | Gly | Glu | Val 200 | Ile | Ala | Thr | Gly | Ser 205 | Met | Asp | Asn |
| 30 | Thr | Ile 210 | Arg | Leu | Trp | Asp | Pro 215 | Lys | Ser | Gly | Gln | Cys 220 | Leu | Gly | Asp | Ala |
| | Leu 225 | Arg | Gly | His | Ser | Lys 230 | Trp | Ile | Thr | Ser | Leu 235 | Ser | Trp | Glu | Pro | Ile 240 |
| 35 | His | Leu | Val | Lys | Pro 245 | Gly | Ser | Lys | | Arg 250 | Leu | Ala | Ser | Ser | Ser 255 | Lys |
| | Asp | Gly | Thr | Ile 260 | Lys | Ile ' | Trp | | Thr ' | Val | Ser | Arg | Val | Cys 270 | Gln | Tyr |
| 40 | Thr | Met | Ser 275 | Gly | His ' | Thr i | | Ser 280 | Val : | Ser | Cys | | Lys 285 | Trp | Gly | Gly |
| 45 | | Gly 290 | Leu | Leu | Tyr : | | Gly : | Ser | His i | Asp . | | Thr | Val | Arg | Val | Trp |
| | Asp | Ile | Asn | Ser | Gln (| Gly 1 | Arg (| Cys | Ile 1 | Asn | Ile 1 | Leu : | Lys | Ser | His | Ala |

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His Trp Val Asn His Leu Ser Leu Ser Thr Asp Tyr Ala Leu Arg Ile Gly Ala Phe Asp His Thr Gly Lys Lys Pro Ser Thr Pro Glu Glu Ala Gln Lys Lys Ala Leu Glu Asn Tyr Glu Lys Ile Cys Lys Lys Asn Gly Asn Ser Glu Glu Met Met Val Thr Ala Ser Asp Asp Tyr Thr Met Phe Leu Trp Asn Pro Leu Lys Ser Thr Lys Pro Ile Ala Arg Met Thr Gly 15. His Gln Lys Leu Val Asn His Val Ala Phe Ser Pro Asp Gly Arg Tyr Ile Val Ser Ala Ser Phe Asp Asn Ser Ile Lys Leu Trp Asp Gly Arg Asp Gly Lys Phe Ile Ser Thr Phe Arg Gly His Ile Ala Ser Val Tyr Gln Val Ala Trp Ser Ser Asp Cys Arg Leu Leu Val Ser Cys Ser Lys Asp Thr Thr Leu Lys Val Trp Asp Val Arg Thr Arg Lys Leu Ser Val -------30 Asp Leu Pro Gly Ile Lys Thr Lys Leu Tyr Val Asp Trp Ser Val Asp Gly Lys Arg Val Cys Ser Gly Gly Lys Asp Lys Met Val Arg Leu Trp Thr His

(2) INFORMATION FOR SEQ ID NO:67:

: 45

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 852 amino acids

(B) TYPE: amino acid

45

| | | | | | | - | 17 | 1 - | | | | | | | | |
|----|--|------------|------------|------------|-----------|------------|------------|------------|------------|-----------|------------|------------|------------|-----|-----------|------------|
| | | (1 | D) T | OPOL | OGY: | unk | nown | | | | | | | | | |
| | (ii) |) MOI | LECU. | LE T | YPE: | pro | tein | | | | | | | | | |
| 5 | (iii) | HYI | POTH | ETICA | AL: 1 | МО | | | | | | | | | | |
| | (iv) | ANT | ri-si | ENSE : | : NO | | | | | | | | | | | |
| 10 | (vi) | ORI | | DIVI | | | LATE | E: YI | CL52! | 5, F: | ig. : | 50 | | | | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:67: | | | | | | | | | | | | | | | |
| 15 | Met 1 | Phe | Lys | Ser | Lys 5 | Thr | Ser | Thr | Leu | Ser 10 | туг | : Asr | o Glu | Thr | Pro |) Asn |
| 20 | Ser | Asn | Glu | Gly 20 | Asp | Arg | Asn | Ala | Thr 25 | Pro | Val | . Asn | Pro | Lys | Glu | Lys |
| 20 | Ser | Gln | Thr 35 | Lys | His | Leu | Asn | Ile 40 | Pro | Gly | Asp | Arg | Ser | Arg | His | Ser |
| 25 | Ser | Ile 50 | Ala | Asp | Ser | Lys | Arg 55 | Ser | Ser | Ser | Arg | Tyr 60 | Asp | Gly | Gly | Tyr |
| | Ser 65 | Ala | Asp | Ile | Ile | Pro 70 | Ala | Gln | Leu | Arg | Phe 75 | Ile | Asp | Asn | Ile | Asp 80 |
| 30 | Tyr | Gly | Thr | Arg | Leu 85 | Arg | Lys | Thr | Leu | His 90 | Arg | Asn | Ser | Val | Val 95 | Ser |
| 35 | Asn | Gly | Tyr | Asn 100 | Lys | Leu | Ser | Glu | Asn 105 | Asp | Arg | Trp | туг | Phe | Asp | Leu |
| | Phe | Asp | Arg 115 | Lys | Tyr | Phe | Glu | Asn 120 | Tyr | Leu | Glu | Glu | Pro 125 | Thr | Tyr | Ile |
| 10 | Lys | Ile 130 | Phe | Lys | Lys | Lys | Glu 135 | Gly | Leu | Glu | Gln | Phe 140 | Asp | Arg | Met | Phe |
| | Leu 145 | Ala | Gln | Glu | Leu | Lys 150 | Ile | Pro | Asp | Val | Tyr 155 | Lys | Ser | Thr | Thr | Tyr 160 |

Gln Gly Glu Pro Ala Val Ala Asn Ser Glu Leu Phe Lys Asn Ser Ile

170

175

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| | | - 17 | 72 - | | |
|----|-----------------------|----------------------|---|----------------------|-------------------|
| | Cys Cys Cys Th | | is Asp Gly Lys 185 | | le Gly Cys 90 |
| 5 | Lys Asp Gly Se | er Leu His Le | eu Trp Lys Val | Ile Asn Ser P | ro Val Lys |
| | Arg Ser Glu Me | | er Glu Lys Ser 15 | Val Ser Ala S 220 | er Arg Ala |
| 10 | Asn Ser Leu Ly 225 | ys Ile Gln A: 230 | rg His Leu Ala | Ser Ile Ser S 235 | er His Asn 240 |
| 15 | Gly Ser Ile Se | er Ser Asn A | sp Leu Lys Pro 250 | Ser Asp Gln P | he Glu Gly 255 |
| | 2 | 60 | eu Tyr Ala Pro 265 | 2 | 70 |
| 20 | 275 | | is Ala Leu Asp 280 | 285 | |
| | 290 | 2 | le Thr Ala Ser 95 | 300 | |
| 25 | 305 | 310 | ys Tyr Ser Leu | 315 | 320 |
| 30 | • | 325 | le Phe Phe Pro | | 335 |
| | 3 | 40 | Ais Arg Cys Arg 345 Phe Asp Cys Lys | 3 | 350 |
| 35 | 355 | | 360 Gly Glu Tyr Thr | 365 | |
| 40 | 370 | 3 | 375 Leu Thr His Gly | 380 | |
| 40 | 385 | 390 | Ser Thr Gln Gly | 395 | 400 |
| 45 | | 405 | 410 Gly Lys Val Glr | ı | 415 |
| | | - | - * | | |

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Gly Leu Gln Cys Phe Phe Ser Lys Val Asp Lys Asn Leu Arg Leu Ile Val Thr Thr Asn Asp Ser Lys Ile Gln Ile Phe Asp Leu Asn Glu Lys Lys Pro Leu Glu Leu Phe Lys Gly Phe Gln Ser Gly Ser Ser Arg His Arg Gly Gln Phe Leu Met Met Lys Asn Glu Pro Val Val Phe Thr Gly Ser Asp Asp His Trp Phe Tyr Thr Trp Lys Met Gln Ser Phe Asn Leu Ser Ala Glu Met Asn Cys Thr Ala Pro His Arg Lys Lys Arg Leu Ser Gly Ser Met Ser Leu Lys Gly Leu Leu Arg Ile Val Ser Asn Lys Ser Thr Asn Asp Glu Cys Leu Thr Glu Thr Ser Asn Gln Ser Ser Ser His Thr Phe Thr Asn Ser Ser Lys Asn Val Leu Gln Thr Gln Thr Val Gly Ser Gln Ala Ile Lys Asn Asn His Tyr Ile Ser Phe His Ala His Asn Ser Pro Val Thr Cys Ala Ser Ile Ala Pro Asp Val Ala Ile Lys Asn Leu Ser Leu Ser Asn Asp Leu Ile Phe Glu Leu Thr Ser Gln Tyr Phe Lys Glu Met Gly Gln Asn Tyr Ser Glu Ser Lys Glu Thr Cys Asp Asn Lys Pro Asn His Pro Val Thr Glu Thr Gly Gly Phe Ser Ser Asn Leu Ser Asn Val Val Asn Asn Val Gly Thr Ile Leu Ile Thr Thr Asp Ser

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Gln Gly Leu Ile Arg Val Phe Arg Thr Asp Ile Leu Pro Glu Ile Arg Lys Lys Ile Ile Glu Lys Phe His Glu Tyr Asn Leu Phe His Leu Glu Ala Ala Gly Lys Ile Asn Asn His Asn Asn Asp Ser Ile Leu Glu Asn Arg Met Asp Glu Arg Ser Ser Thr Glu Asp Asn Glu Phe Ser Thr Thr Pro Pro Ser Asn Thr His Asn Ser Arg Pro Ser His Asp Phe Cys Glu 15.. . Leu His Pro Asn Asn Ser Pro Val Ile Ser Gly Met Pro Ser Arg Ala Ser Ala Ile Phe Lys Asn Ser Ile Phe Asn Lys Ser Asn Gly Ser Phe Ile Ser Leu Lys Ser Arg Ser Glu Ser Thr Ser Ser Thr Val Phe Gly Pro His Asp Ile Pro Arg Val Ser Thr Thr Tyr Pro Lys Leu Lys Cys Asp Val Cys Asn Gly Ser Asn Phe Glu Cys Ala Ser Lys Asn Pro Ile Ala Gly Gly Asp Ser Gly Phe Thr Cys Ala Asp Cys Gly Thr Ile Leu Asn Asn Phe Arg (2) INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 798 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: protein

45 (iii) HYPOTHETICAL: NO

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195

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| | | | | | | | Τ, | | | | | | | | | |
|----|------------|-------------|-------------|------------|------------|------------|------------|------------|-------------|------------|------------|------------|------------|------------|-------------|------------|
| | (iv | ı) Al | NTI-S | ENSE | E: NC |) | | | | | | | | | | |
| r | (vi | | | AL S | | | OLAT | Е: у | rb 1 | 410 | yeas | st, I | Fig. | 51 | | |
| 5 | | | | | | | | | | | | | | | | • |
| | (xi |) SE | QUEN | CE D | ESCR | IPTI | ON: | SEQ | ID N | iO:68 | 3: | | | | | |
| 10 | Me 1 | t Se | r Gl | n Ly | s Gl: 5 | n Se: | r Th | r As | n Gl | n As | | n As | n Gl | y Th | ır Hi 15 | s Gln |
| | Pr | o Gl | n Pro | o Va: | l Lys | a Ası | n Glr | ı Ar | g Th: 25 | r As | n As: | n Al | a Al | a Gl 30 | y Al | a Asn |
| 15 | Se | r Gl | y Gli 35 | n Glr | n Pro | Gln | ı Glr | Glr 40 | ı Sei | r Glı | n Gly | y Gli | n Se 45 | r Gl: | n Gl: | n Gln |
| 20 | Gly | y Arg 50 | g Ser | Asr. | Gly | Pro | Phe 55 | Ser | ` Ala | a Ser | c Asp | Let 60 | ı Ası | n Arg | g Ile | e Val |
| | Leu 65 | ı Glu | ı Tyr | Leu | Asn | Lys 70 | Lys | Gly | Tyr | His | Arg 75 | Thr | Glu | ı Ala | . Met | Leu 80 |
| 25 | Arg | Ala | Glu | Ser | Gly 85 | Arg | Thr | Leu | Thr | Pro | Gln | Asn | Lys | Gln | Ser 95 | Pro |
| | Ala | Asn | Thr | Lys 100 | Thr | Gly | Lys | Phe | Pro 105 | Glu | Gln | Ser | Ser | Ile | Pro | Pro |
| 30 | Asn | Pro | Gly 115 | Lys | Thr | Ala | Lys | Pro 120 | Ile | Ser | Asn | Pro | Thr 125 | | Leu | Ser |
| 35 | Ser | Lys 130 | Arg | Asp | Ala | Glu | Gly 135 | Gly | Ile | Val | Ser | Ser 140 | Gly | Arg | Leu | Glu |
| | Gly 145 | Leu | Asn | Ala | Pro | Glu 150 | Asn | Tyr | Ile | Arg | Ala 155 | Tyr | Ser | Met | Leu | Lys 160 |
| 40 | Asn | Trp | Val | Asp | Ser 165 | Ser | Leu | Glu | Ile | Tyr 170 | Lys | Pro | Glu | Leu | Ser 175 | Tyr |
| | Ile | Met | Tyr | Pro 180 | Ile | Phe | Ile ' | | Leu 185 | Phe | Leu | Asn | Leu | Val | Ala | Lys |

Asn Pro Val Tyr Ala Arg Arg Phe Phe Asp Arg Phe Ser Pro Asp Phe

205

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| | | | | | | -] | .76 | - | | | | | | | | |
|---------|-------------|------------|-------------|------------|--------------|--------------|--------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| | Lys | Asp 210 | Phe | His | Gly | | Glu : 215 | Ile | Asn | Arg | | Phe 220 | Ser | Val | Asn | Ser |
| 5 | Ile 225 | Asp | His | Ile | | Glu . 230 | Asn (| Glu | Val | Ala | Ser 235 | Ala | Phe | Gln | Ser | His 240 |
| | Lys | Tyr | Arg | Ile | Thr 245 | Met | Ser | Lys | Thr | Thr 250 | Leu | Asn | Leu | Leu | Leu 255 | Tyr |
| 10 | Phe | Leu | Asn | Glu 260 | Asn | Glu | Ser | Ile | Gly 265 | Gly | Ser | Leu | Ile | Ile 270 | Ser | Val |
| u un la | Ile | Asn | Gln 275 | His | Leu | Asp | | Asn 280 | Ile | Val | Glu | Ser | Val 285 | Thr | Ala | Arg |
| 15 | Glu | Lys 290 | | Ala | Asp | Gly | Ile 295 | Lys | Val | Leu | Ser | Asp 300 | Ser | Glu | Asn | Gly |
| 20 | Asn 305 | | / Lys | Gln | Asn | Leu 310 | Glu | Met | Asn | Ser | Val 315 | Pro | Val | Lys | Leu | Gly 320 |
| | Pro | Phe | e Pro | Lys | Asp 325 | Glu | Glu | Phe | Val | Lys 330 | Glu | Ile | Glu | Thr | Glu 335 | Leu |
| 25 | Lys | ; Ile | e Lys | Asp 340 | | Gln | Glu | Lys | Gln 345 | | Asn | Gln | Gln | Thr 350 | Ala | Gly |
| 30-4 | Ası |) As | n Ty: | r Ser | : Gly | Ala | Asn | Asn 360 | | Thr | Leu | Leu | Gln 365 | Glu | Tyr | Lys |
| 30 | Ala | a Me 37 | | n Asr | n Glu | Lys | Phe 375 | | Asp | Asn | Thr | Gly 380 | | Asp | Asp | Lys |
| 35 | As ; | _ | s Il | e Ly: | s Asr | 390 | | Ala | Lys | : Asp | 395 | | Lys | Lys | Glu | 400 |
| | Gl | u Le | u Ly | s Va | 1 Ası 409 | | , Glu | Lys | . Lys | Asr 410 | | Ası | n Lev | ser | Ser 415 | Pro |
| 40 | Al | a Ar | g As | p Il 42 | | ŭ Pro | Lev | ı Pro | 42 | | s Thi | Ala | a Leu | 430 | | ı Lys |
| 45 | L€ | eu Gl | lu II 43 | | n Ly | s Va | l Lys | 44 | | r Arg | g Ası | o Ala | 44! | | s Le | u Asp |
| | As | en L | eu G | ln Le | u Al | a Le | u Pro | o Se | r Va | l Cy | s Me | t Ty | r Th | r Ph | e Gl | n Asn |

- 177 -Thr Asn Lys Asp Met Ser Cys Leu Asp Phe Ser Asp Asp Cys Arg Ile Ala Ala Gly Phe Gln Asp Ser Tyr Ile Lys Ile Trp Ser Leu Asp Gly Ser Ser Leu Asn Asn Pro Asn Ile Ala Leu Asn Asn Asn Asp Lys Asp Glu Asp Pro Thr Cys Lys Thr Leu Val Gly His Ser Gly Thr Val Tyr Ser Thr Ser Phe Ser Pro Asp Asn Lys Tyr Leu Leu Ser Gly Ser Glu Asp Lys Thr Val Arg Leu Trp Ser Met Asp Thr His Thr Ala Leu Val Ser Tyr Lys Gly His Asn His Pro Val Trp Asp Val Ser Phe Ser Pro Leu Gly His Tyr Phe Ala Thr Ala Ser His Asp Gln Thr Ala Arg Leu Trp Ser Cys Asp His Ile Tyr Pro Leu Arg Ile Phe Ala Gly His Leu Asn Asp Val Asp Cys Val Ser Phe His Pro Asn Gly Cys Tyr Val Phe Thr Gly Ser Ser Asp Lys Thr Cys Arg Met Trp Asp Val Ser Thr Gly Asp Ser Val Arg Leu Phe Leu Gly His Thr Ala Pro Val Ile Ser Ile Ala Val Cys Pro Asp Gly Arg Trp Leu Ser Thr Gly Ser Glu Asp Gly Ile Ile Asn Val Trp Asp Ile Gly Thr Gly Lys Arg Leu Lys Gln

Met Arg Gly His Gly Lys Asn Ala Ile Tyr Ser Leu Ser Tyr Ser Lys

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Glu Gly Asn Val Leu Ile Ser Gly Gly Ala Asp His Thr Val Arg Val 715 710 705 Trp Asp Leu Lys Lys Ala Thr Thr Glu Pro Ser Ala Glu Pro Asp Glu 730 725 5 Pro Phe Ile Gly Tyr Leu Gly Asp Val Thr Ala Ser Ile Asn Gln Asp 750 745 740 Ile Lys Glu Tyr Gly Arg Arg Thr Val Ile Pro Thr Ser Asp Leu 10 765 760 755 Val Ala Ser Phe Tyr Thr Lys Lys Thr Pro Val Phe Lys Val Lys Phe 3 - 43 775 770 15 Ser Arg Ser Asn Leu Ala Leu Ala Gly Gly Ala Phe Arg Pro 795 790 785 (2) INFORMATION FOR SEQ ID NO:69: 20 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 25 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 30 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RACK1 protein rI, Fig. 1C 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:69: Gly His Asn Gly Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro 15 10 5 40 1 Asp Met Ile Leu Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys 30 25 20

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(2) INFORMATION FOR SEQ ID NO:70:

40

45

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(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 5 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 10 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RACK1 protein rII, Fig. 1C 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:70: Gly His Ser His Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln 20 Phe Ala Leu Ser Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp 25 (2) INFORMATION FOR SEQ ID NO:71: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 35 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RACK1 protein rIII, Fig. 1C (xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

Gly His Thr Lys Asp Val Leu Ser Val Ala Phe Ser Ser Asp Asn Arg

Gln Ile Val Ser Gly Ser Arg Asp Lys Thr Ile Lys Leu Trp Asn

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20 25 30

(2) INFORMATION FOR SEQ ID NO:72:

5 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

10 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

15

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: RACK1 protein rIV, Fig. 1C

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser Ser 1 5 10 15

Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val Trp 20 25 30

Asn

30

(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

35 (B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

40 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

45 (C) INDIVIDUAL ISOLATE: RACK1 protein rV, Fig. 1C

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

Gly His Thr Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser

1 10 15

5

Leu Cys Ala Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp

(2) INFORMATION FOR SEQ ID NO:74:

10

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

15

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 20 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RACK1 protein rVI, Fig. 1C

25

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys Phe Ser Pro Asn Arg

30

Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile Lys Ile Trp Asp

(2) INFORMATION FOR SEQ ID NO:75:

35

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 45 (iv) ANTI-SENSE: NO

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(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: RACK1 protein rVII, Fig. 1C

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75: 5

> Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser Leu Ala Trp Ser Ala Asp 10 5 1

Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp Asn Leu Val Arg Val Trp 10 25 20

Gln

15

- (2) INFORMATION FOR SEQ ID NO:76:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
- (B) TYPE: amino acid 20
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO 25
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- (C) INDIVIDUAL ISOLATE: Human 55 kDa protein rI, Fig. 11 30
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:
- Gly His Thr Asp Ala Val Leu Asp Leu Ser Trp Asn Lys Leu Ile Arg 35 5

Asn Val Leu Ala Ser Ala Ser Ala Asp Asn Thr Val Ile Leu Trp Asp 30 25 20

- (2) INFORMATION FOR SEQ ID NO:77:
 - (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 32 amino acids 45
 - (B) TYPE: amino acid

- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- 5 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 10 (C) INDIVIDUAL ISOLATE: Human 55 kDa protein rII, Fig. 11
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:
- Ala His Asn Asp Glu Ile Ser Gly Leu Asp Leu Ser Ser Gln Ile Lys

 1 5 10 15
- Gly Cys Leu Val Thr Ala Ser Ala Asp Lys Tyr Val Lys Ile Trp Asp
 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:78:
 - (i) SEQUENCE CHARACTERISTICS:
- 25 (A) LENGTH: 37 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 30

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 35 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: Human 55 kDa protein rIII, Fig. 11
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:
- Val His Ser Arg Asp Met Lys Met Gly Val Leu Phe Cys Ser Ser Cys

 1 5 10
- Cys Pro Asp Leu Pro Phe Ile Tyr Ala Phe Gly Gly Gln Lys Glu Gly
 20 25 30

Leu Arg Val Trp Asp 35

(2) INFORMATION FOR SEQ ID NO:79:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO 15
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: AAC-RICH protein rI, Fig. 12

20

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:
- Gly Asn Lys Lys Ser Thr Ser Val Ala Trp Asn Ala Asn Gly Thr 10 5

25

- Lys Ile Ala Ser Ser Gly Ser Asp Gly Ile Val Arg Val Trp Asn 25 20
- (2) INFORMATION FOR SEQ ID NO:80:

3.0

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

35

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO 40
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: AAC-RICH protein rII, Fig. 12

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

5

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Gly His Asp Gly Ser Ile Glu Lys Ile Ser Trp Ser Pro Lys Asn Asn 1 5 10 15

Asp Leu Leu Ala Ser Ala Gly Thr Asp Lys Val Ile Lys Ile Trp Asp 20 25 30

- (2) INFORMATION FOR SEQ ID NO:81:
- 10 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 15 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
- 20
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: AAC-RICH protein rIII, Fig. 12
- 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

Asp His Leu Ala Leu Ile Asp Leu Pro Thr Ile Lys Thr Leu Lys Ile 1 5 10 15

- Tyr Lys Phe Asn Gly Glu Glu Leu Asn Gln Val Gly Trp Asp
 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:82:
- 35 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 40 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
- 45
- (vi) ORIGINAL SOURCE:

15

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- (C) INDIVIDUAL ISOLATE: AAC-RICH protein rIV, Fig. 12
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

Gly His Thr Ala Ser Ile Tyr Cys Met Glu Phe Asp Pro Thr Gly Lys
1 5 10 15

Tyr Leu Ala Ala Gly Ser Ala Asp Ser Ile Val Ser Leu Trp Asp
20 25 30

- (2) INFORMATION FOR SEQ ID NO:83:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 34 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide

20 (iii) HYPOTHETICAL: NO

- (iv) ANTI-SENSE: NO
- 25 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: BETA TRCP rI, Fig. 13
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

30

Ile His Cys Arg Ser Glu Thr Ser Lys Gly Val Tyr Cys Leu Gln Tyr

1 5 10 15

Asp Asp Gln Lys Ile Val Ser Gly Leu Arg Asp Asn Thr Ile Lys Ile
25 30

Trp Asp

- 40 (2) INFORMATION FOR SEQ ID NO:84:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 28 amino acids
 - (B) TYPE: amino acid
- 45 (D) TOPOLOGY: unknown

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```
(ii) MOLECULE TYPE: peptide
          (iii) HYPOTHETICAL: NO
         (iv) ANTI-SENSE: NO
           (vi) ORIGINAL SOURCE:
                 (C) INDIVIDUAL ISOLATE: BETA TRCP rII, Fig. 13
 10
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:
           Gly His Thr Gly Ser Val Leu Cys Leu Gln Tyr Asp Glu Arg Val Ile
                           5
                                                10
                                                                    15
 15
           Ile Thr Gly Ser Asp Ser Thr Val Arg Val Trp Asp
                       20
      (2) INFORMATION FOR SEQ ID NO:85:
20
           (i) SEQUENCE CHARACTERISTICS:
                (A) LENGTH: 30 amino acids
                (B) TYPE: amino acid
                (D) TOPOLOGY: unknown
25
         (ii) MOLECULE TYPE: peptide
        (iii) HYPOTHETICAL: NO
30
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
               (C) INDIVIDUAL ISOLATE: BETA TRCP rIII, Fig. 13
35
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:
         Ile His His Cys Glu Ala Val Leu His Leu Arg Phe Asn Asn Gly Met
                          5
                                              10
40
         Met Val Thr Cys Ser Lys Asp Arg Ser Ile Ala Val Trp Asp
                      20
                                          25
```

(2) INFORMATION FOR SEQ ID NO:86:

45

(i) SEQUENCE CHARACTERISTICS:

- 188 -(A) LENGTH: 29 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: BETA TRCP rIV, Fig. 13 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:86: 15.... Gly His Arg Ala Ala Val Asn Val Val Asp Phe Asp Asp Lys Tyr Ile 10 5 Val Ser Ala Ser Gly Asp Arg Thr Ile Lys Val Trp Asn 20 25 20 (2) INFORMATION FOR SEQ ID NO:87: (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 29 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 30 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 35 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: BETA TRCP rV, Fig. 13 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:87: 40 Gly His Lys Arg Gly Ile Ala Cys Leu Gln Tyr Arg Asp Arg Leu Val 15 10 5

Val Ser Gly Ser Ser Asp Asn Thr Ile Arg Leu Trp Asp 45 25 20

- (2) INFORMATION FOR SEQ ID NO:88:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 29 amino acids
- 5 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: BETA TRCP rVI, Fig. 13
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:
- Gly His Glu Glu Leu Val Arg Cys Ile Arg Phe Asp Asn Lys Arg Ile

 1 5 10 15

Val Ser Gly Ala Tyr Asp Gly Lys Ile Lys Val Trp Asp 20 25

- (2) INFORMATION FOR SEQ ID NO:89:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 29 amino acids
- 30 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 35 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 40 (C) INDIVIDUAL ISOLATE: BETA TRCP rVII, Fig. 13
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:
- Glu His Ser Gly Arg Val Phe Arg Leu Gln Phe Asp Glu Phe Gln Ile

 1 5 10 15

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Val Ser Ser His Asp Asp Thr Ile Leu Ile Trp Asp
20 25

(2) INFORMATION FOR SEQ ID NO:90:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: beta-prime-cop rI, Fig. 14

20

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:
- Ala His Ser Asp Tyr Ile Arg Cys Ile Ala Val His Pro Thr Gln Pro 1 5 10 15

25

- Phe Ile Leu Thr Ser Ser Asp Asp Met Leu Ile Lys Leu Trp Asp
 20 25 30
- (2) INFORMATION FOR SEQ ID NO:91:

30...

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

35

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 40 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: beta-prime-cop rII, Fig. 14

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

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Gly His Thr His Tyr Val Met Gln Ile Val Ile Asn Pro Lys Asp Asn

1 10 15

Asn Gln Phe Ala Ser Ala Ser Leu Asp Arg Thr Ile Lys Val Trp Gln
5 20 25 30

- (2) INFORMATION FOR SEQ ID NO:92:
- 10 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 15 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

20

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: beta-prime-cop rIII, Fig. 14
- 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

Gly His Glu Lys Gly Val Asn Cys Ile Asp Tyr Tyr Ser Gly Gly Asp

1 10 15

Lys Pro Tyr Leu Ile Ser Gly Ala Asp Asp Arg Leu Val Lys Ile Trp
20 25 30

Asp

35

- (2) INFORMATION FOR SEQ ID NO:93:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 45 (iii) HYPOTHETICAL: NO

- 192 -

| | (iv) ANTI-SENSE: NO |
|----|---|
| | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: beta-prime-cop rIV, Fig. 14</pre> |
| 5 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:93: |
| | Gly His Ala Gln Asn Val Ser Cys Ala Ser Phe His Pro Glu Leu Pro 1 5 10 15 |
| 10 | Ile Ile Ile Thr Gly Ser Glu Asp Gly Thr Val Arg Ile Trp His 20 25 30 |
| | (2) INFORMATION FOR SEQ ID NO:94: |
| 15 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 30 amino acids(B) TYPE: amino acid |
| | (D) TOPOLOGY: unknown |
| 20 | (ii) MOLECULE TYPE: peptide |
| | (iii) HYPOTHETICAL: NO |
| 25 | (iv) ANTI-SENSE: NO |
| | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CDC4 / CDC20 protein rI, Fig. 15</pre> |
| 30 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:94: |
| | Gly His Met Thr Ser Val Ile Thr Cys Leu Gln Phe Glu Asp Asn Tyr 1 5 10 15 |
| 35 | Val Ile Thr Gly Ala Asp Asp Lys Met Ile Arg Val Tyr Asp 20 25 30 |
| | (2) INFORMATION FOR SEQ ID NO:95: |
| 40 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 30 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| 45 | |

(ii) MOLECULE TYPE: peptide

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| | (iii) HYPOTHETICAL: NO |
|----|---|
| | (iv) ANTI-SENSE: NO |
| 5 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CDC4 / CDC20 protein rII, Fig. 1</pre> |
| 10 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:95: |
| | Gly His Asp Gly Gly Val Trp Ala Leu Lys Tyr Ala His Gly Gly II |
| 15 | Leu Val Ser Gly Ser Thr Asp Arg Thr Val Arg Val Trp Asp 20 25 30 |
| | (2) INFORMATION FOR SEQ ID NO:96: |
| 20 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 33 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| 25 | (ii) MOLECULE TYPE: peptide |
| | (iii) HYPOTHETICAL: NO |
| 30 | (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CDC4 / CDC20 protein rIII, Fig. 15 |
| 35 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:96: |
| | Gly His Asn Ser Thr Val Arg Cys Leu Asp Ile Val Glu Tyr Lys Asn 1 5 10 15 |
| 40 | Ile Lys Tyr Ile Val Thr Gly Ser Arg Asp Asn Thr Leu His Val Trp 20 25 30 |
| | Lys |

45 (2) INFORMATION FOR SEQ ID NO:97:

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(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 29 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 5 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CDC4 / CDC20 protein rIV, Fig. 15 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:97: Gly His Met Ala Ser Val Arg Thr Val Ser Gly His Gly Asn Ile Val 10 20 Val Ser Gly Ser Tyr Asp Asn Thr Leu Ile Val Trp Asp (2) INFORMATION FOR SEQ ID NO:98: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 35 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CDC4 / CDC20 protein rV, Fig. 15 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:98: Gly His Thr Asp Arg Ile Tyr Ser Thr Ile Tyr Asp His Glu Arg Lys 10 45 Arg Cys Ile Ser Ala Ser Met Asp Thr Thr Ile Arg Ile Trp Asp

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- (2) INFORMATION FOR SEQ ID NO:99:
- 5 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 29 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 10 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

15

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: CDC4 / CDC20 protein rVI, Fig. 15
- 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:
 - Gly His Thr Ala Leu Val Gly Leu Leu Arg Leu Ser Asp Lys Phe Leu

 1 5 10 15
- Val Ser Ala Ala Ala Asp Gly Ser Ile Arg Gly Trp Asp
 20 25
 - (2) INFORMATION FOR SEQ ID NO:100:
- 30 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 35 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: GBLP-CHLAMIDOMONAS HOMOLOG rI, Fig. 16
- 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

- 196 -Gly His Thr Asn Trp Val Thr Ala Ile Ala Thr Pro Leu Asp Pro Ser 10 Ser Asn Thr Leu Leu Ser Ala Ser Arg Asp Lys Ser Val Leu Val Trp 25 5 Glu (2) INFORMATION FOR SEQ ID NO:101: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 15 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBLP -CHLAMIDOMONAS HOMOLOG rII, Fig. 25 16 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:101: Gly His Ser His Phe Val Gln Asp Val Val Ile Ser Ser Asp Gly Gln 30 10 5 Phe Cys Leu Thr Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp 30 25 20 35 (2) INFORMATION FOR SEQ ID NO:102: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid 40 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

- 197 -

- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: GBLP -CHLAMIDOMONAS HOMOLOG rIII, Fig.

5 16

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:
- Gly His Thr Lys Asp Val Leu Ser Val Ala Phe Ser Val Asp Asn Arg

 10 1 5 10 15
 - Gln Ile Val Ser Gly Ser Arg Asp Lys Thr Ile Lys Leu Trp Asn 20 25 30
- 15 (2) INFORMATION FOR SEQ ID NO:103:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 amino acids
 - (B) TYPE: amino acid
- 20 (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO

25

- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: GBLP -CHLAMIDOMONAS HOMOLOG rIV, Fig.

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:
- Gly His Thr Glu Trp Val Ser Cys Val Arg Phe Ser Pro Met Thr Thr

 1 5 10 15
 - Asn Pro Ile Ile Val Ser Gly Gly Trp Asp Lys Met Val Lys Val Trp 20 25 30
- 40 Asn
 - (2) INFORMATION FOR SEQ ID NO:104:
- 45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 31 amino acids

| | - 196 - | • |
|----|---|----|
| | (B) TYPE: amino acid | |
| | (D) TOPOLOGY: unknown | |
| 5 | (ii) MOLECULE TYPE: peptide | |
| J | (iii) HYPOTHETICAL: NO | |
| | (iv) ANTI-SENSE: NO | |
| 10 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBLP -CHLAMIDOMONAS HOMOLOG rV, Fig.</pre> | |
| | 16 | |
| 15 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:104: | |
| | Gly His His Gly Tyr Val Asn Thr Val Thr Val Ser Pro Asp Gly Ser 1 10 15 | |
| 20 | Leu Cys Ala Ser Gly Gly Lys Asp Gly Ile Ala Met Leu Trp Asp 20 25 30 | |
| | (2) INFORMATION FOR SEQ ID NO:105: | |
| 25 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 32 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown | |
| 30 | (ii) MOLECULE TYPE: peptide | |
| | (iii) HYPOTHETICAL: NO | |
| 35 | (iv) ANTI-SENSE: NO | |
| | (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBLP - CHLAMIDOMONAS HOMOLOG rVI, Fig | į. |
| | 16 | |
| 40 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:105: | |
| | Ile His Cys Leu Cys Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala 1 5 10 15 | |
| 45 | | |

Thr Gln Ser Ser Ile Lys Ile Trp Asp Leu Glu Ser Lys Ser Ile Val

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(2) INFORMATION FOR SEQ ID NO:106: 5 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 33 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 10 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 15 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GBLP -CHLAMIDOMONAS HOMOLOG rVII, Fig. 16 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:106: Lys Lys Ala Gln Val Pro Tyr Cys Val Ser Leu Ala Trp Ser Ala Asp 25 Gly Ser Thr Leu Tyr Ser Gly Tyr Thr Asp Gly Gln Ile Arg Val Trp 20 25 30 30 Ala (2) INFORMATION FOR SEQ ID NO:107:

35 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 33 amino acids

- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown
- 40 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

45

(vi) ORIGINAL SOURCE:

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(C) INDIVIDUAL ISOLATE: cop-1 protein rI, Fig. 17

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

Met Ser Thr Arg Ser Lys Leu Ser Cys Leu Ser Trp Asn Lys His Glu 1 5 10 15

Lys Asn His Ile Ala Ser Ser Asp Tyr Glu Gly Ile Val Thr Val Trp
20 25 30

Asp

- 15 (2) INFORMATION FOR SEQ ID NO:108:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 amino acids
 - (B) TYPE: amino acid
- 20 (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO

25

5

- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: cop-1 protein rII, Fig. 17

30

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:
- Glu Lys Arg Ala Trp Ser Val Asp Phe Ser Arg Thr Glu Pro Ser Met

 1 5 10 15

Leu Val Ser Gly Ser Asp Asp Cys Lys Val Lys Val Trp Cys
20 25 30

- 40 (2) INFORMATION FOR SEQ ID NO:109:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 amino acids
 - (B) TYPE: amino acid
- 45 (D) TOPOLOGY: unknown

- 201 -

- (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 5 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: cop-1 protein rIII, Fig. 17 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:109: Gly His Lys Lys Ala Val Ser Tyr Met Lys Phe Leu Ser Asn Asn Glu 15 15 Leu Ala Ser Ala Ser Thr Asp Ser Thr Leu Arg Leu Trp Asp 20 25 30 (2) INFORMATION FOR SEQ ID NO:110: 20 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 25 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 30 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Coronin (p55) rI, Fig. 19 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:110: Gly His Lys Ser Ala Val Leu Asp Ile Ala Phe His Pro Phe Asn Glu 5 Asn Leu Val Gly Ser Val Ser Glu Asp Cys Asn Ile Cys Ile Trp Gly 20
- 45 (2) INFORMATION FOR SEQ ID NO:111:

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| | | | | | | | 202 | | | | | | | | | |
|----|----------|-------------|-------|--------------|--------------|-------------|--------|-----------|-------|-----------|-------|-------|-------|------|-------------|-----|
| | (i) | (B) | | GTH: E: a | 32 mino | amin aci | o ac | | | | | | | | | |
| 5 | (ii) | MOLE | CULE | TYP | E: p | epti | .de | | | | | | | | | |
| | (iii) | НУРС | THET | 'ICAL | : NC |) | | | | | | | | | | |
| 10 | (iv) | ANTI | -SEN | SE: | NO | | | | | | | | | | | |
| | (vi) | ORIG (C) | | | | | LATE : | : Cor | onir | ı (p | 55) r | :II, | Fig. | 19 | | |
| 15 | (xi) | SEQU | JENCI | DES | SCRII | PTIO | N: SI | EQ II | ONO: | :111 | : | | | | | |
| | _ | His | Lys | Arg | Lys 5 | Val | Gly | Thr | Ile | Ser 10 | Phe | Gly | Pro | Val | Ala 15 | Asp |
| 20 | 1 | | | | | | | 61 | | | T 011 | vol | Two | Thr | Trn | Aen |
| | Asn | Val | Ala | Val 20 | Tnr | ser | ser | GIY | 25 | File | Беа | Val | цуз | 30 | 115 | |
| 25 | (2) INFO | RMAT | ION 1 | FOR (| SEQ | ID N | 0:11 | 2 : | | | | | | | | |
| 30 | (i) | (B | | NGTH PE : | : 31 amin | ami o ac | no a | | | | | | | | | |
| | (ii) |) MOL | ECUL | E TY | PE: | pept | ide | | | | | | | | | |
| 35 | (iii) |) HYP | OTHE | TICA | L: N | O | | | | | | | | | | |
| 33 | (iv |) ANI | I-SE | NSE: | ио | | | | | | | | | | | |
| 40 | (vi | ORI | | | | | OLATE | E: Co | roni | n (r | 55) | rIII | , Fi | g. 1 | .9 | |
| | |) SEÇ | | | | | | | | | | | | | | |
| | | y His | s Sei | : Ası | | t Ile | e Thi | r Sei | c Cys | | ı TrŢ |) Ası | n His | AST | ı Gly 15 | seı |
| 45 | 1 | | | | 5 | | | | | 10 | | | | | | |

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Gln Ile Val Thr Thr Cys Lys Asp Lys Lys Ala Arg Val Phe Asp 20 25 30

(2) INFORMATION FOR SEQ ID NO:113:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 38 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: CORO PROTEIN rI, Fig. 18

20

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:113:
- Arg His Val Phe Ala Ala Gln Pro Lys Lys Glu Glu Cys Tyr Gln Asn
 1 5 10 15

25

30

35

Leu Lys Thr Lys Ser Ala Val Trp Asp Ser Asn Tyr Val Ala Ala Asn 20 25 30

Thr Arg Tyr Ile Trp Asp 35

- (2) INFORMATION FOR SEQ ID NO:114:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 45 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: CORO PROTEIN rII, Fig. 18

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| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:114: | |
|----------|---|---|
| 5 | Gly His Lys Ser Ala Val Leu Asp Ile Ala Phe His Pro Phe Asn Glu 1 5 10 15 | |
| | Asn Leu Val Gly Ser Val Ser Glu Asp Cys Asn Ile Cys Ile Trp Gly 20 25 30 | |
| 10 | (2) INFORMATION FOR SEQ ID NO:115: | |
| 15 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 32 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown | |
| | (ii) MOLECULE TYPE: peptide | |
| 20 | (iii) HYPOTHETICAL: NO | |
| | (iv) ANTI-SENSE: NO | |
| 25 | (vi) ORIGINAL SOURCE:(C) INDIVIDUAL ISOLATE: CORO PROTEIN rIII, Fig. 18 | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:115: | |
| 30 | Gly His Lys Arg Lys Val Gly Thr Ile Ser Phe Gly Pro Val Ala As 1 5 10 15 | Ş |
| <u>.</u> | Asn Val Ala Val Thr Ser Ser Gly Asp Phe Leu Val Lys Thr Trp As | P |
| 35 | | |
| | (2) INFORMATION FOR SEQ ID NO:116: | |
| 40 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 29 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown | |

(iii) HYPOTHETICAL: NO

45

(ii) MOLECULE TYPE: peptide

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- (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CORO PROTEIN rIV, Fig. 18 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:116: Gly His Ser Asp Met Ile Thr Ser Cys Glu His Asn Gly Ser Gln Ile 10 1 10 Val Thr Thr Cys Lys Asp Lys Lys Ala Arg Val Phe Asp 20 15 (2) INFORMATION FOR SEQ ID NO:117: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid 20 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 25 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CSTF 50kDa rI, Fig. 20 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:117: Asp His Val Asp Glu Val Thr Cys Leu Ala Phe His Pro Thr Glu Gln 35 5 Ile Leu Ala Ser Gly Ser Arg Asp Tyr Thr Leu Lys Leu Phe Asp 20 30 40 (2) INFORMATION FOR SEQ ID NO:118:
- - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
- 45 (D) TOPOLOGY: unknown

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| | (ii) | MOLECULE TYPE: peptide |
|----|----------|--|
| | (iii) | HYPOTHETICAL: NO |
| 5 | (iv) | ANTI-SENSE: NO |
| | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CSTF 50kDa rII, Fig. 20 |
| 10 | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:118: |
| | Asp 1 | His Val Asp Glu Val Thr Cys Leu Ala Phe His Pro Thr Glu Gln 5 10 15 |
| 15 | Ile | Leu Ala Ser Gly Ser Arg Asp Tyr Thr Leu Lys Leu Phe Asp 20 25 30 |
| 20 | (2) INFO | RMATION FOR SEQ ID NO:119: |
| 25 | (i) | SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| | (ii) | MOLECULE TYPE: peptide |
| 30 | (iii) | HYPOTHETICAL: NO |
| | (iv) | ANTI-SENSE: NO |
| | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CSTF 50kDa rIII, Fig. 20 |
| 35 | | |
| | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:119: |
| 40 | Ala 1 | a His Asp Gly Ala Glu Val Cys Ser Ala Ile Phe Ser Lys Asn Ser 5 10 15 |
| | Ly | s Tyr Ile Leu Ser Ser Gly Lys Asp Ser Val Ala Lys Leu Trp Gl |
| | | |

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(2) INFORMATION FOR SEQ ID NO:120:

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- 207 -(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 29 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 5 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CSTF 50kDa rIV, Fig. 20 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:120: Val His Arg Thr Gln Ala Val Phe Asn His Thr Glu Asp Tyr Val Leu 20 Leu Pro Asp Glu Arg Thr Ile Ser Leu Cys Cys Trp Asp 20 (2) INFORMATION FOR SEQ ID NO:121: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 35 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: CSTF 50kDa rV, Fig. 20 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:121: Gly His Asn Asn Ile Val Arg Cys Ile Val His Ser Pro Thr Asn Pro 5 10 15

Gly Phe Met Thr Cys Ser Asp Asp Phe Arg Ala Arg Phe Trp Tyr

20 25 30

| (2) | INFORMATION | FOR | SEQ | ID | NO:122 |
|-----|-------------|-----|-----|----|--------|
|-----|-------------|-----|-----|----|--------|

- 5 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 10 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

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- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: G- BETA DROSOPH rI, Fig. 23
- 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:122:

Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Gly Asn Asp Ser Arg

1 10 15

- Asn Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile Val Trp Asp
 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:123:
- 30 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 35 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: G- BETA DROSOPH rII, Fig. 23
- 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:123:

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- 209 -Gly His Gly Gly Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Gln 10 Ile Val Thr Ser Ser Gly Asp Met Ser Cys Gly Leu Trp Asp 5 20 25 (2) INFORMATION FOR SEQ ID NO:124: (i) SEQUENCE CHARACTERISTICS: 10 (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G- BETA DROSOPH rIII, Fig. 23 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:124: Gly His Thr Gly Asp Val Met Ala Leu Ser Leu Ala Pro Gln Cys Lys 10 15 Thr Phe Val Ser Gly Ala Cys Asp Ala Ser Ala Lys Leu Trp Asp 20

- (2) INFORMATION FOR SEQ ID NO:125:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE: 45
 - (C) INDIVIDUAL ISOLATE: G- BETA DROSOPH rIV, Fig. 23

- 210 -(xi) SEQUENCE DESCRIPTION: SEQ ID NO:125: Gly His Glu Ser Asp Ile Asn Ala Val Thr Phe Phe Pro Asn Gly Gln 10 5 5 Ala Phe Ala Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp 25 (2) INFORMATION FOR SEQ ID NO:126: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 34 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 15 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 20 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G- BETA DROSOPH rV, Fig. 23 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:126: 25 Ser His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ala Phe Ser Lys 10 5 Ser Gly Arg Leu Leu Ala Gly Tyr Asp Asp Phe Asn Cys Asn Val 30 30 25 20 Trp Asp 35 (2) INFORMATION FOR SEQ ID NO:127: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid 40 (D) TOPOLOGY: unknown

45 (iii) HYPOTHETICAL: NO

(ii) MOLECULE TYPE: peptide

- 211 -

| | - 211 - |
|----|---|
| | (iv) ANTI-SENSE: NO |
| 5 | (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G- BETA DROSOPH rVI, Fig. 23 |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:127: |
| 10 | Gly His Asp Asn Arg Val Ser Cys Leu Gly Val Thr Glu Asn Gly Met 1 5 10 15 |
| | Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu Arg Val Trp Asn 20 25 30 |
| 15 | (2) INFORMATION FOR SEQ ID NO:128: |
| 20 | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid |
| 20 | (D) TOPOLOGY: unknown |
| | (ii) MOLECULE TYPE: peptide |
| 25 | (iii) HYPOTHETICAL: NO |
| | (iv) ANTI-SENSE: NO |
| 30 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rI, Fig. 24</pre> |
| 30 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:128: |
| 35 | Gly His Asn Gly Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro 1 5 10 15 |
| | Asp Met Ile Leu Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys 20 25 30 |

- 40 (2) INFORMATION FOR SEQ ID NO:129:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
- 45 (D) TOPOLOGY: unknown

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(ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rII, Fig. 24 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:129: Gly His Ser His Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln 10 15 Phe Ala Leu Ser Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp 25 (2) INFORMATION FOR SEQ ID NO:130: 20 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 25 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 30-(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rIII, Fig. 24 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:130: Gly His Thr Lys Asp Val Leu Ser Val Ala Phe Ser Ser Asp Asn Arg 40 Gln Ile Val Ser Gly Ser Arg Asp Lys Thr Ile Lys Leu Trp Asn 30 20 (2) INFORMATION FOR SEQ ID NO:131: 45

(i) SEQUENCE CHARACTERISTICS:

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- 213 -(A) LENGTH: 33 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 5 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rIV, Fig. 24 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:131: 15 Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser Ser 1 -10 15 Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val Trp 20 20 25 30 Asn 25 (2) INFORMATION FOR SEQ ID NO:132: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 35 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rV, Fig. 24 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:132: Gly His Thr Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser 45 1 5

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Leu Cys Ala Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp
20 25 30

(2) INFORMATION FOR SEQ ID NO:133:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 36 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

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- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rVI, Fig. 24

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- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:133:
- Lys His Leu Tyr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys

 1 10 15

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Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile 20 25 30

Lys Ile Trp Asp

30

35

- (2) INFORMATION FOR SEQ ID NO:134:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide

40

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 45 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: G-BETA HUMAN rVII, Fig. 24

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:134: Ala Glu Pro Pro Gln Cys Thr Ser Leu Ala Trp Ser Ala Asp Gly Gln 10 Thr Leu Phe Ala Gly Tyr Thr Asp Asn Leu Val Arg Val Trp Gln 25 10 (2) INFORMATION FOR SEQ ID NO:135: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid 15 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta 1 bovine rI, Fig. 21 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:135: Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Gly Thr Asp Ser Arg 30 10 15 Leu Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile Ile Trp Asp 20 25 30 -35 (2) INFORMATION FOR SEQ ID NO:136: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid 40 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide

(iv) ANTI-SENSE: NO

45

(iii) HYPOTHETICAL: NO

| | - 216 - |
|------------|---|
| | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta 1 bovine rII, Fig. 21</pre> |
| 5 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:136: |
| | Gly His Thr Gly Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Gln 1 10 15 |
| 10 | Ile Val Thr Ser Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp 20 25 30 |
| | (2) INFORMATION FOR SEQ ID NO:137: |
| 15 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 31 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| 20 | (ii) MOLECULE TYPE: peptide |
| | (iii) HYPOTHETICAL: NO |
| 25 | (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: |
| | (C) INDIVIDUAL ISOLATE: G-Beta 1 bovine rIII, Fig. 21 |
| 30 .tcm | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:137: |
| | Gly His Thr Gly Asp Val Met Ser Leu Ser Leu Ala Pro Asp Thr Arg 1 5 10 15 |
| 35 | Leu Phe Val Ser Gly Ala Cys Asp Ala Ser Ala Lys Leu Trp Asp 20 25 30 |
| | (2) INFORMATION FOR SEQ ID NO:138: |
| 40 | (i) SEQUENCE CHARACTERISTICS: |

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

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| | (iii) | HYPOTHETICAL: NO |
|----|----------|--|
| | (iv) | ANTI-SENSE: NO |
| 5 | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta 1 bovine rIV, Fig. 21 |
| 10 | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:138: |
| | Gly 1 | His Glu Ser Asp Ile Asn Ala Ile Cys Phe Phe Pro Asn Gly Asn 5 10 15 |
| 15 | Ala | Phe Ala Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp 20 25 30 |
| | (2) INFO | RMATION FOR SEQ ID NO:139: |
| 20 | (i) | SEQUENCE CHARACTERISTICS: (A) LENGTH: 34 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| 25 | | MOLECULE TYPE: peptide |
| | | HYPOTHETICAL: NO |
| 30 | | ORIGINAL SOURCE: |
| | | (C) INDIVIDUAL ISOLATE: G-Beta 1 bovine rV, Fig. 21 |
| 35 | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:139: |
| | Ser 1 | His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ser Phe Ser Lys 5 10 15 |
| 40 | Ser | Gly Arg Leu Leu Ala Gly Tyr Asp Asp Phe Asn Cys Asn Val 20 25 30 |
| | Trp | Asp |

45 (2) INFORMATION FOR SEQ ID NO:140:

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| | | - 210 - |
|-------------|-----------------------|--|
| | (i) | SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| 5 | (ii) | MOLECULE TYPE: peptide |
| | (iii) | HYPOTHETICAL: NO |
| 10 | (iv) | ANTI-SENSE: NO |
| | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta 1 bovine rVI, Fig. 21 |
| 15 | | |
| | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:140: |
| | Gly 1 | His Asp Asn Arg Val Ser Cys Leu Gly Val Thr Asp Asp Gly Met 5 10 15 |
| 20 | Ala | Val Ala Thr Gly Ser Trp Asp Ser Phe Leu Lys Ile Trp Asn 20 25 30 |
| | | |
| | (2) INFO | RMATION FOR SEQ ID NO:141: |
| 25 | | SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| 2.5 3.0 | (i) | SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid |
| | (i) (ii) | SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| | (i) (ii) (iii) | SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown MOLECULE TYPE: peptide |
| 3.0 | (ii) (iii) (iv) | SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown MOLECULE TYPE: peptide HYPOTHETICAL: NO |
| 3.0 | (ii) (iii) (iv) (vi) | SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown MOLECULE TYPE: peptide HYPOTHETICAL: NO ANTI-SENSE: NO ORIGINAL SOURCE: |
| 3.0. 3.5 | (ii) (iii) (iv) (vi) | SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown MOLECULE TYPE: peptide HYPOTHETICAL: NO ANTI-SENSE: NO ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta-bovine(2) rI, Fig. 22 |

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(2) INFORMATION FOR SEQ ID NO:142:

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5 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 30 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

10 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

15

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: G-Beta-bovine(2) rII, Fig. 22

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:142:

Gly His Thr Gly Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Gln

1 10 15

25 Ile Ile Thr Ser Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp 20 25 30

(2) INFORMATION FOR SEQ ID NO:143:

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

35 (ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

40

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: G-Beta-bovine(2) rIII, Fig. 22

45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:143:

- 220 -Gly His Ser Gly Asp Val Met Ser Leu Ser Leu Ala Pro Asp Gly Arg Thr Phe Val Ser Gly Ala Cys Asp Ala Ser Ile Lys Leu Trp Asp 25 20 5 (2) INFORMATION FOR SEQ ID NO:144: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids 10 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 15 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 20 (C) INDIVIDUAL ISOLATE: G-Beta-bovine(2) rIV, Fig. 22 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:144: 25 Gly His Glu Ser Asp Ile Asn Ala Val Ala Phe Phe Pro Asn Gly Tyr 10 Ala Phe Thr Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp 20 30 (2) INFORMATION FOR SEQ ID NO:145: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 34 amino acids 35 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 40 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 45

(C) INDIVIDUAL ISOLATE: G-Beta-bovine(2) rV, Fig. 22

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14% Ser His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ala Phe Ser Arg 5 10 Ser Gly Arg Leu Leu Ala Gly Tyr Asp Asp Phe Asn Cys Asn Ile 20 25 30 10 Trp Asp (2) INFORMATION FOR SEQ ID NO:146: 15 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 20 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 25 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta-bovine(2) rVI, Fig. 22 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:146: 30 Gly His Asp Asn Arg Val Ser Cys Leu Gly Val Thr Asp Asp Gly Met 1 5 10 Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu Lys Ile Trp Asn 35 20 25 30 (2) INFORMATION FOR SEQ ID NO:147: (i) SEQUENCE CHARACTERISTICS: 40 (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

| | - 222 - |
|----|---|
| | (iv) ANTI-SENSE: NO |
| 5 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta2(Human) rI, Fig. 25</pre> |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:147: |
| 10 | Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Gly Thr Asp Ser Arg 1 5 10 15 |
| | Leu Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile Ile Trp Asp 20 25 30 |
| 15 | (2) INFORMATION FOR SEQ ID NO:148: |
| 20 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 30 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| | (ii) MOLECULE TYPE: peptide |
| 25 | (iii) HYPOTHETICAL: NO |
| | (iv) ANTI-SENSE: NO |
| 30 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta2(Human) rII, Fig. 25</pre> |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:148: |
| 35 | Gly His Thr Gly Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Gln 1 5 10 15 |
| | Ile Ile Thr Ser Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp 20 25 30 |
| 40 | (2) INFORMATION FOR SEQ ID NO:149: |
| | (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids |

(B) TYPE: amino acid(D) TOPOLOGY: unknown

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(ii) MOLECULE TYPE: peptide
         (iii) HYPOTHETICAL: NO
        (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
                (C) INDIVIDUAL ISOLATE: G-Beta2(Human) rIII, Fig. 25
10
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:149:
          Gly His Ser Gly Asp Val Met Ser Leu Ser Leu Ala Pro Asp Gly Arg
                          5
                                                                    15
15
          Thr Phe Val Ser Gly Ala Cys Asp Ala Ser Ile Lys Leu Trp Asp
                      20
                                           25
     (2) INFORMATION FOR SEQ ID NO:150:
20
          (i) SEQUENCE CHARACTERISTICS:
               (A) LENGTH: 31 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: unknown
25
         (ii) MOLECULE TYPE: peptide
        (iii) HYPOTHETICAL: NO
30
         (iv) ANTI-SENSE: NO
         (vi) ORIGINAL SOURCE:
               (C) INDIVIDUAL ISOLATE: G-Beta2(Human) rIV, Fig. 25
35
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:150:
          Gly His Glu Ser Asp Ile Asn Ala Val Ala Phe Phe Pro Asn Gly Tyr
                                               10
40
          Ala Phe Thr Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp
                      20
                                          25
     (2) INFORMATION FOR SEQ ID NO:151:
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(i) SEQUENCE CHARACTERISTICS:

10

- 224 -(A) LENGTH: 34 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta2(Human) rV, Fig. 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:151: 15 Ser His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ala Phe Ser Arg 15 10 5 Ser Gly Arg Leu Leu Leu Ala Gly Tyr Asp Asp Phe Asn Cys Asn Ile 20 30 20 25 Trp Asp 25 (2) INFORMATION FOR SEQ ID NO:152: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid 30 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta2(Human) rVI, Fig. 25 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:152: Gly His Asp Asn Arg Val Ser Cys Leu Gly Val Thr Asp Asp Gly Met 45

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Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu Lys Ile Trp Asn 20 25 30

(2) INFORMATION FOR SEQ ID NO:153:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

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- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: G-Beta4 (mouse) rI, Fig. 26

20

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:153:
- Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Gly Tyr Asp Ser Arg

 1 5 10 15

25

- Leu Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile Ile Trp Asp
 20 25 30
- (2) INFORMATION FOR SEQ ID NO:154:

30

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

35

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 40 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: G-Beta4(mouse) rII, Fig. 26

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:154:

- 226 -Gly His Thr Gly Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Gly Gln 10 Ile Ile Thr Ser Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp 25 20 5 (2) INFORMATION FOR SEQ ID NO:155: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids 10 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 15 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 20 (C) INDIVIDUAL ISOLATE: G-Beta4(mouse) rIII, Fig. 26 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:155: Gly His Ser Gly Asp Val Met Ser Leu Ser Leu Ser Pro Asp Leu Lys 15 5 Thr Phe Val Ser Gly Ala Cys Asp Ala Ser Ser Lys Leu Trp Asp 25 30 30 20 (2) INFORMATION FOR SEQ ID NO:156: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids 35 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 40 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO

(C) INDIVIDUAL ISOLATE: G-Beta4 (mouse) rIV, Fig. 26

(vi) ORIGINAL SOURCE:

- 227 -

| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:156: |
|----|---|
| 5 | Gly His Ile Ser Asp Ile Asn Ala Val Ser Phe Phe Pro Ser Gly Tyr 1 5 10 15 |
| | Ala Phe Ala Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp 20 25 30 |
| 10 | (2) INFORMATION FOR SEQ ID NO:157: |
| 15 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 34 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| | (ii) MOLECULE TYPE: peptide |
| 20 | (iii) HYPOTHETICAL: NO |
| | (iv) ANTI-SENSE: NO |
| 25 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta4(mouse) rV, Fig. 26</pre> |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:157: |
| 30 | Ser His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ala Phe Ser Lys 1 10 15 |
| | Ser Gly Arg Leu Leu Ala Gly Tyr Asp Asp Phe Asn Cys Ser Val 20 25 30 |
| 35 | Trp Asp |
| | (2) INFORMATION FOR SEQ ID NO:158: |
| 40 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 31 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |

45 (ii) MOLECULE TYPE: peptide

- 228 -

| | (iii) HYPOTHETICAL: NO |
|-----|---|
| | (iv) ANTI-SENSE: NO |
| 5 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: G-Beta4(mouse) rVI, Fig. 26</pre> |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:158: |
| 10 | Gly His Asp Asn Arg Val Ser Cys Leu Gly Val Thr Asp Asp Gly Met 1 5 10 15 |
| 1-5 | Ala Val Ala Thr Gly Ser Trp Asp Ser Phe Leu Arg Ile Trp Asn 20 25 30 |
| | (2) INFORMATION FOR SEQ ID NO:159: |
| 20 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 31 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| 25 | (ii) MOLECULE TYPE: peptide |
| 25 | (iii) HYPOTHETICAL: NO |
| | (iv) ANTI-SENSE: NO |
| 30 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GROUCHO PROT. DRSPH rI, Fig. 27</pre> |
| 35 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:159: |
| | Thr Ser Ala Ala Pro Ala Cys Tyr Ala Leu Ala Ser Pro Asp Ser Lys 1 5 10 15 |
| 40 | Val Cys Phe Ser Cys Cys Ser Asp Gly Asn Ile Ala Val Trp Asp 20 25 30 |
| | (2) INFORMATION FOR SEQ ID NO:160: |

(i) SEQUENCE CHARACTERISTICS:

45

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- 5 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 10 (C) INDIVIDUAL ISOLATE: GROUCHO PROT. DRSPH rII, Fig. 27
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:160:
- Gly His Thr Asp Gly Ala Ser Cys Ile Asp Ile Ser Pro Asp Gly Ser

 1 5 10 15
 - Arg Leu Trp Thr Gly Gly Leu Asp Asn Thr Val Arg Ser Trp Asp
 20 25 30

- (2) INFORMATION FOR SEQ ID NO:161:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
- 25 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 30 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 35 (C) INDIVIDUAL ISOLATE: GTP binding prt squid rI, Fig. 28
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:161:
- Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Ala Ser Asp Ser Arg

 1 5 10 15
 - Asn Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile Val Trp Asp 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:162:

| | - 230 - |
|----|---|
| | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 30 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| 5 | (ii) MOLECULE TYPE: peptide |
| | (iii) HYPOTHETICAL: NO |
| 10 | (iv) ANTI-SENSE: NO |
| | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GTP binding prt squid rII, Fig. 28</pre> |
| 15 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:162: |
| 20 | Gly His Thr Gly Tyr Leu Ser Cys Cys Arg Phe Ile Asp Asp Asn Gln 1 5 10 15 |
| 20 | Ile Val Thr Ser Ser Gly Asp Met Thr Cys Ala Leu Trp Asn 20 25 30 |
| 25 | (2) INFORMATION FOR SEQ ID NO:163: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids |
| | (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| 30 | (ii) MOLECULE TYPE: peptide |
| | (iii) HYPOTHETICAL: NO |
| 35 | (iv) ANTI-SENSE: NO |
| | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GTP binding prt squid rIII, Fig. 28</pre> |
| 40 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:163: |
| | Gly His Thr Gly Asp Val Met Ser Leu Ser Leu Ala Pro Asp Met Arg |

Thr Phe Val Ser Gly Ala Cys Asp Ala Ser Ala Lys Leu Phe Asp

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20

25

30

- (2) INFORMATION FOR SEQ ID NO:164:
- 5 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 10 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

15

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: GTP binding prt squid rIV, Fig. 28
- 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:164:

Gly His Glu Ser Asp Ile Asn Ala Ile Thr Tyr Phe Pro Asn Gly Phe 1 5 10 15

- Ala Phe Ala Thr Gly Ser Asp Asp Ala Thr Cys Arg Leu Phe Asp
 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:165:
- 30 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 34 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 35 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: GTP binding prt squid rV, Fig. 28
- 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:165:

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Ser His Asp Asn Ile Ile Cys Gly Ile Thr Ser Val Ala Phe Ser Lys 10 Ser Gly Arg Leu Leu Gly Gly Tyr Asp Asp Phe Asn Cys Asn Val 30 25 20 Trp Asp (2) INFORMATION FOR SEQ ID NO:166: 10 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 24 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 15 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: GTP binding prt squid rVI, Fig. 28 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:166: Gly His Asp Asn Arg Val Ser Cys Leu Gly Val Thr Glu Asp Gly Met 10 30 Ala Val Ala Thr Gly Ser Trp Asp 20 (2) INFORMATION FOR SEQ ID NO:167: 35 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 40 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

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- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: IEF SSP 9306 rI, Fig. 29
- 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:167:
 - Gly His Gln Lys Glu Gly Tyr Gly Leu Ser Trp Asn Pro Asn Leu Ser 1 5 10 15
- 10 Gly His Leu Leu Ser Ala Ser Asp Asp His Thr Ile Cys Leu Trp Asp 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:168:

15

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

20

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 25 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: IEF SSP 9306 rII, Fig. 29

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:168:

Gly His Thr Ala Val Val Glu Asp Val Ser Trp His Leu Leu His Glu

1 10 15

- Ser Leu Phe Gly Ser Val Ala Asp Asp Gln Lys Leu Met Ile Trp Asp 20 25 30
- 40 (2) INFORMATION FOR SEQ ID NO:169:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 37 amino acids
 - (B) TYPE: amino acid
- 45 (D) TOPOLOGY: unknown

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| | (ii) MOLECULE TYPE: peptide |
|-----|---|
| | (iii) HYPOTHETICAL: NO |
| 5 | (iv) ANTI-SENSE: NO |
| | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: IEF SSP 9306 rIII, Fig. 29</pre> |
| 10 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:169: |
| | Ser His Ser Val Asp Ala His Thr Ala Glu Val Asn Cys Leu Ser Phe 1 10 15 |
| 15 | Asn Pro Tyr Ser Glu Phe Ile Leu Ala Thr Gly Ser Ala Asp Lys Thr 20 25 30 |
| 20 | Val Ala Leu Trp Asp 35 |
| | (2) INFORMATION FOR SEQ ID NO:170: |
| 25 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 37 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| 30 | (ii) MOLECULE TYPE: peptide |
| | (iii) HYPOTHETICAL: NO |
| | (iv) ANTI-SENSE: NO |
| 35 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: IEF SSP 9306 rIV, Fig. 29</pre> |
| 40 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:170: |
| - • | Leu His Ser Phe Glu Ser His Lys Asp Glu Ile Phe Gln Val Gln Trp 1 5 10 15 |
| 45 | Ser Pro His Asn Glu Thr Ile Leu Ala Ser Ser Gly Thr Asp Arg Arg |

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Leu Asn Val Trp Asp 35

(2) INFORMATION FOR SEQ ID NO:171:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 34 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: IEF SSP 9306 rV, Fig. 29

20

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:171:

25

Leu Leu Phe Ile His Gly Gly His Thr Ala Lys Ile Ser Asp Phe Ser 20 25 30

Trp Asn

30

- (2) INFORMATION FOR SEQ ID NO:172:
 - (i) SEQUENCE CHARACTERISTICS:

35

- (A) LENGTH: 32 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 45
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: HUMAN 12.3 rI, Fig. 30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:172: Gly His Asn Gly Trp Val Thr Gln Ile Ala Thr Thr Pro Gln Phe Pro 10 5 5 Asp Met Ile Leu Ser Ala Ser Arg Asp Lys Thr Ile Ile Met Trp Lys 30 25 20 10 (2) INFORMATION FOR SEQ ID NO:173: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid 15 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: HUMAN 12.3 rII, Fig. 30 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:173: Gly His Ser His Phe Val Ser Asp Val Val Ile Ser Ser Asp Gly Gln 30 10 5 Phe Ala Leu Ser Gly Ser Trp Asp Gly Thr Leu Arg Leu Trp Asp 30 25 20 35 (2) INFORMATION FOR SEQ ID NO:174: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid 40 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide

45 (iii) HYPOTHETICAL: NO

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- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: HUMAN 12.3 rIII, Fig. 30

5

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:174:
- Gly His Thr Lys Asp Val Leu Ser Val Ala Phe Ser Ser Asp Asn Arg

 10 1 5 10 15

Gln Ile Val Ser Gly Ser Arg Asp Lys Thr Ile Lys Leu Trp Asn 20 25 30

- 15 (2) INFORMATION FOR SEQ ID NO:175:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 amino acids
 - (B) TYPE: amino acid
- 20 (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO

25

- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: HUMAN 12.3 rIV, Fig. 30

30

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:175:

Ser His Ser Glu Trp Val Ser Cys Val Arg Phe Ser Pro Asn Ser Ser 35 1 5 10 15

Asn Pro Ile Ile Val Ser Cys Gly Trp Asp Lys Leu Val Lys Val Trp 20 25 30

40 Asn

- (2) INFORMATION FOR SEQ ID NO:176:
- 45 (i) SEQUENCE CHARACTERISTICS:
 (A) LENGTH: 31 amino acids

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(B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 5 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 10 (C) INDIVIDUAL ISOLATE: HUMAN 12.3 rV, Fig. 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:176: 15 Gly His Thr Gly Tyr Leu Asn Thr Val Thr Val Ser Pro Asp Gly Ser 10 5 Leu Cys Ala Ser Gly Gly Lys Asp Gly Gln Ala Met Leu Trp Asp 25 20 20 (2) INFORMATION FOR SEQ ID NO:177: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 36 amino acids 25 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 30 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: HUMAN 12.3 rVI, Fig. 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:177: 40 Lys His Leu Tyr Thr Leu Asp Gly Gly Asp Ile Ile Asn Ala Leu Cys 10 15 5 1 Phe Ser Pro Asn Arg Tyr Trp Leu Cys Ala Ala Thr Gly Pro Ser Ile

25

20

Lys Ile Trp Asp 35

(2) INFORMATION FOR SEQ ID NO:178:

5

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 38 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

10

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

15 (iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: HUMAN 12.3 rVII, Fig. 30

20 -

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:178:

Val Ile Ser Thr Ser Ser Lys Ala Glu Pro Pro Gln Cys Thr Ser Leu 1 5 10 15

25

Ala Trp Ser Ala Asp Gly Gln Thr Leu Phe Ala Gly Tyr Thr Asp Asn 20 25 30

Leu Val Arg Val Trp Gln

30 35

- (2) INFORMATION FOR SEQ ID NO:179:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 32 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

40

35

(iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

45 (vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: IEF-7442-human rI, Fig. 31

(iii) HYPOTHETICAL: NO

| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:179: | |
|-----|---|---|
| 5 | Gly His Gln Lys Glu Gly Tyr Gly Leu Ser Trp Asn Ser Asn Leu Ser 1 5 10 15 | |
| | Gly His Leu Leu Ser Ala Ser Asp Asp His Thr Val Cys Leu Trp Asp 20 25 30 | |
| 10 | (2) INFORMATION FOR SEQ ID NO:180: | |
| 15 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 32 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown | |
| | (ii) MOLECULE TYPE: peptide | |
| 20 | (iii) HYPOTHETICAL: NO | |
| | (iv) ANTI-SENSE: NO | |
| 25 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: IEF-7442-human rII, Fig. 31</pre> | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:180: | |
| 3.0 | Gly His Ser Ala Val Val Glu Asp Val Ala Trp His Leu Leu His Glu 1 5 10 15 | 1 |
| | Ser Leu Phe Gly Ser Val Ala Asp Asp Gln Lys Leu Met Ile Trp Asp 20 25 30 | Þ |
| 35 | | |
| | (2) INFORMATION FOR SEQ ID NO:181: | |
| 40 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 32 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown | |
| | (ii) MOLECULE TYPE: peptide | |

- 241 -(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: IEF-7442-human rIII, Fig. 31 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:181: Ala His Thr Ala Glu Val Asn Cys Leu Ser Phe Asn Pro Tyr Ser Glu 10 1 5 Phe Ile Leu Ala Thr Gly Ser Ala Asp Lys Thr Val Ala Leu Trp Asp 20 25 15 (2) INFORMATION FOR SEQ ID NO:182: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 24 amino acids 20 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 30 (C) INDIVIDUAL ISOLATE: IEF-7442-human rIV, Fig. 31 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:182: Val His Trp Ser Pro His Asn Glu Thr Ile Leu Ala Ser Ser Gly Thr 35 1 5 10 15 Asp Arg Arg Leu Asn Val Trp Asp 20 40 (2) INFORMATION FOR SEQ ID NO:183:

(i) SEQUENCE CHARACTERISTICS:

(B) TYPE: amino acid (D) TOPOLOGY: unknown

45

(A) LENGTH: 32 amino acids

| | (ii) | MOLECULE TY | PE: pept | ide | | | | | | | | |
|-----|----------|--|-----------------------|---------|--------------|-------------|-------|-------|-------|-----------|-------------|-----|
| | (iii) | HYPOTHETICA | L: NO | | | | | | | | | |
| 5 | (iv) | ANTI-SENSE: | ИО | | | | | | | | | |
| | (vi) | ORIGINAL SO | | LATE: I | EF-744 | 12-hu | man 1 | cV, : | Fig. | 31 | | |
| LO | (xi) | SEQUENCE DE | SCRIPTIO | N: SEQ | ID NO: | :183: | | | | | | |
| | Gly 1 | His Thr Ala | Lys Ile 5 | Ser As | p Phe | Ser 10 | Trp 1 | Asn | Pro l | | Glu 1 15 | Pro |
| 1.5 | Trp | Val Ile Cys 20 | Ser Val | Ser Gl | u Asp 25 | Asn | Ile : | Met | | Ile 30 | Trp (| Gln |
| 20 | (2) INFO | RMATION FOR | SEQ ID N | 10:184: | | | | | | | | |
| 25 | (i) | SEQUENCE CH (A) LENGTH (B) TYPE: (D) TOPOLO | H: 32 ami amino ad | no acid | ls | | | | | | | |
| | (ii) | MOLECULE T | YPE: pept | ide | | | | | | | | |
| 30 | (iii) | нүротнетіс | AL: NO | | | | | | | • | | |
| 30 | (iv) | ANTI-SENSE | : NO | | | | | | | | | |
| | (vi) | ORIGINAL S | IDUAL IS | | | | ke GF | bir | nding | ı | | |
| 35 | | pr | otein co | mplex r | I, Fig | , 32 | | | | | | |
| | (xi) | SEQUENCE D | ESCRIPTI | ON: SEQ | ID NO | 0:184 | : | | | | | |
| 40 | Ala 1 | His Thr Pr | o Ala Le 5 | u Ala S | er Leu | ı Gly 10 | Leu | Ser | Asn | Asn | Arg 15 | Leu |
| | Sei | r Arg Leu Gl | | y Leu P | he Glu 25 | ı Gly | Leu | Gly | Ser | Leu 30 | Trp | Asp |
| | | | | | | | | | | | | |

(2) INFORMATION FOR SEQ ID NO:185:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
- 5 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: Insulin-like growth factor bind.
 pro. complex-rat rI, Fig. 33
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:185:
- Thr His Thr Pro Ser Leu Ala Ser Leu Ser Leu Ser Ser Asn Leu Leu

 1 5 10 15
 - Gly Arg Leu Glu Glu Gly Leu Phe Gln Gly Leu Ser His Leu Trp Asp
 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:186:
 - (i) SEQUENCE CHARACTERISTICS:
- 30 (A) LENGTH: 47 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 35 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
- 40 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: Insulin-like growth factor bind. pro. complex-rat rII, Fig. 33
- 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:186:

WO 95/21252 PCT/US95/01210

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Asn His Leu Glu Thr Leu Ala Glu Gly Leu Phe Ser Ser Leu Gly Arg

1 10 15

Val Arg Tyr Leu Ser Leu Arg Asn Ser Leu Gln Thr Phe Ser Pro 20 25 30

Gln Pro Gly Leu Glu Arg Leu Trp Leu Asp Ala Asn Pro Trp Asp 35 40 45

- 10 (2) INFORMATION FOR SEQ ID NO:187:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
- 15 (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO

20

- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: LIS1 (human) rI, Fig. 34

25

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:187:
- Gly His Arg Ser Pro Val Thr Arg Val Ile Phe His Pro Val Phe Ser

Val Met Val Ser Ala Ser Glu Asp Ala Thr Ile Lys Val Trp Asp
20 25 30

- 35 (2) INFORMATION FOR SEQ ID NO:188:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
- 40 (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO

45

(iv) ANTI-SENSE: NO

- 245 -

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: LIS1 (human) rII, Fig. 34
- 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:188:

Gly His Thr Asp Ser Val Gln Asp Ile Ser Phe Asp His Ser Gly Lys

1 10 15

- Leu Leu Ala Ser Cys Ser Ala Asp Met Thr Ile Lys Leu Trp Asp
 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:189:
- 15 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 20 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

25

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: LIS1 (human) rIII, Fig. 34
- 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:189:

Gly His Asp His Asn Val Ser Ser Val Ala Ile Met Pro Asn Gly Asp 1 5 10 15

- 35 His Ile Val Ser Ala Ser Arg Asp Lys Thr Ile Lys Met Trp Glu 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:190:
- 40 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 45 (ii) MOLECULE TYPE: peptide

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| | - |
|----|---|
| | (iii) HYPOTHETICAL: NO |
| | (iv) ANTI-SENSE: NO |
| 5 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: LIS1 (human) rIV, Fig. 34</pre> |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:190: |
| 10 | Gly His Arg Glu Trp Val Arg Met Val Arg Pro Asn Gln Asp Gly Thr 1 5 10 15 |
| 15 | Leu Ile Ala Ser Cys Ser Asn Asp Gln Thr Val Arg Val Trp Val 20 25 30 |
| | (2) INFORMATION FOR SEQ ID NO:191: |
| 20 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 26 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| | (ii) MOLECULE TYPE: peptide |
| 25 | (iii) HYPOTHETICAL: NO |
| | (iv) ANTI-SENSE: NO |
| 30 | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: LIS1 (human) rV, Fig. 34</pre> |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:191: |
| 35 | Gly Ser Glu Thr Lys Lys Ser Gly Lys Pro Gly Pro Phe Leu Leu Ser |
| 40 | Gly Ser Arg Asp Lys Thr Lys Met Trp Asp 20 25 |
| | (2) INFORMATION FOR SEQ ID NO:192: |
| | (i) SEQUENCE CHARACTERISTICS: |

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

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(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

5 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

10 (C) INDIVIDUAL ISOLATE: LIS1 (human) rVI, Fig. 34

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:192:

Gly His Asp Asn Trp Val Arg Gly Val Leu Phe His Ser Gly Gly Lys

1 5 10 15

Phe Ile Leu Ser Cys Ala Asp Asp Lys Thr Leu Arg Val Trp Asp 20 25 30

20

45

(2) INFORMATION FOR SEQ ID NO:193:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

25 (B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

30 (iii) HYPOTHETICAL: NO

(iv) ANTI-SENSE: NO

(vi) ORIGINAL SOURCE:

35 (C) INDIVIDUAL ISOLATE: LIS1 (human) rVII, Fig. 34

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:193:

Ala His Glu His Phe Val Thr Ser Leu Asp Phe His Lys Thr Ala Pro

1 5 10 15

Tyr Val Val Thr Gly Ser Val Asp Gln Thr Val Lys Val Trp Glu 20 25 30

(2) INFORMATION FOR SEQ ID NO:194:

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(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 29 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 5 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: MD6 rI, Fig. 35 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:194: Gly His Ser Ala Arg Val Tyr Ala Leu Tyr Tyr Lys Asp Gly Leu Leu 10 20 Cys Thr Gly Ser Asp Asp Leu Ser Ala Lys Leu Trp Asp 25 20 (2) INFORMATION FOR SEQ ID NO:195: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 27 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown - 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 35 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: MD6 rII, Fig. 35 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:195: Thr His Thr Cys Ala Ala Val Lys Phe Asp Glu Gln Lys Leu Val Thr 15 10 5 45

Gly Ser Phe Asp Asn Thr Val Ala Cys Trp Glu

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20

25

| (2) | INFORMATION | FOR | SEQ | ID | NO:196: |
|-----|-------------|-----|-----|----|---------|
|-----|-------------|-----|-----|----|---------|

- 5 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 10 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

15

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: MD6 rIII, Fig. 35
- 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:196:
 - Gly His Thr Gly Ala Val Phe Ser Val Asp Tyr Ser Asp Glu Leu Asp 1 5 10 15
- 25 Ile Leu Val Ser Gly Ser Ala Asp Phe Ala Val Lys Val Trp Ala 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:197:
- 30 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 40 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 35 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: MD6 rIV, Fig. 35
- 45 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:197:

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Gly His Thr Glu Trp Val Thr Lys Val Val Leu Gln Lys Cys Lys Val 1 5 10 15

Lys Ser Leu Leu His Ser Pro Gly Asp Tyr Ile Leu Leu Ser Ala Asp
5 20 25 30

Lys Tyr Glu Ile Lys Ile Trp Pro 35 40

- 10 (2) INFORMATION FOR SEQ ID NO:198:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
- 15 (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO

20

- (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: MSL1 rI, Fig. 36

25

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:198:
- Lys His Asp Gly Gly Val Asn Ser Cys Arg Phe Asn Tyr Lys Asn Ser

 10 15
 - Leu Ile Leu Ala Ser Ala Asp Ser Asn Gly Arg Leu Asn Leu Trp Asp
 20 25 30

35

- (2) INFORMATION FOR SEQ ID NO:199:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 amino acids
- (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 45 (iii) HYPOTHETICAL: NO

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(iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: MSL1 rII, Fig. 36 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:199: Glu His Gly Thr Ser Val Ser Thr Leu Glu Trp Ser Pro Asn Phe Asp 10 10 Thr Val Leu Ala Thr Ala Gly Gln Glu Asp Gly Leu Val Lys Leu Trp 25 15 Asp (2) INFORMATION FOR SEQ ID NO:200: (i) SEQUENCE CHARACTERISTICS: 20 (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 25 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 30 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: MSL1 rIII, Fig. 36 35 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:200: Gly His Met Leu Gly Val Asn Asp Ile Ser Trp Asp Ala His Asp Pro 5 10 Trp Leu Met Cys Ser Val Ala Asn Asp Asn Ser Val His Ile Trp Lys 40 20 25 30

(2) INFORMATION FOR SEQ ID NO:201:

45

(i) SEQUENCE CHARACTERISTICS:

| | | - 252 - |
|-----|----------|---|
| | | (A) LENGTH: 31 amino acids (B) TYPE: amino acid |
| | | (D) TOPOLOGY: unknown |
| 5 | (ii) | MOLECULE TYPE: peptide |
| | (iii) | HYPOTHETICAL: NO |
| 10 | (iv) | ANTI-SENSE: NO |
| | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: MUS MUSCULUS PROTEIN rI, Fig. 37 |
| 15 | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:201: |
| | Gly | His Ser Gly Cys Val Asn Thr Val His Phe Asn Gln His Gly Thr |
| | 1 | 5 10 15 |
| 20 | Leu | Leu Ala Ser Gly Ser Asp Asp Leu Lys Val Ile Val Trp Asp 20 25 30 |
| | | |
| | (2) INFO | RMATION FOR SEQ ID NO:202: |
| 25 | (i) | SEQUENCE CHARACTERISTICS: |
| | | (A) LENGTH: 50 amino acids |
| | | (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| | | (b) Toponogi. Wikilowii |
| 3.0 | (ii) | MOLECULE TYPE: peptide |
| | (iii) | HYPOTHETICAL: NO |
| 35 | (iv) | ANTI-SENSE: NO |
| | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: MUS MUSCULUS PROTEIN rII, Fig. 37 |
| 40 | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:202: |
| | Gly | His Ile Phe Ile Trp Glu Lys Ser Ser Cys Gln Ile Val Gln Phe |
| | 1 | 5 10 15 |
| 45 | Leı | Glu Ala Asp Glu Gly Gly Thr Ile Asn Cys Ile Asp Ser His Pro |

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Tyr Leu Pro Val Leu Ala Ser Ser Gly Leu Asp His Glu Val Lys Ile 35 40 45

Trp Ser

5 50

- (2) INFORMATION FOR SEQ ID NO:203:
- 10 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 15 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

20

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: ORF RB1 rI, Fig. 38
- 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:203:

Lys His Asp Gly Gly Val Asn Ser Cys Arg Phe Asn Tyr Lys Asn Ser 1 5 10 15

- Leu Ile Leu Ala Ser Ala Asp Ser Asn Gly Arg Leu Asn Leu Trp Asp
 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:204:

35

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 33 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 45 (iv) ANTI-SENSE: NO

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- (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: ORF RB1 rII, Fig. 38 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:204: Glu His Gly Thr Ser Val Ser Thr Leu Glu Trp Ser Pro Asn Phe Asp 10 Thr Val Leu Ala Thr Ala Gly Gln Glu Asp Gly Leu Val Lys Leu Trp 10 25 Asp 15. (2) INFORMATION FOR SEQ ID NO:205: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid 20 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 25 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: ORF RB1 rIII, Fig. 38 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:205: Gly His Met Leu Gly Val Asn Asp Ile Ser Trp Asp Ala His Asp Pro 35 10 5 Trp Leu Met Cys Ser Val Ala Asn Asp Asn Ser Val His Ile Trp Lys 30 25 20 40
 - (2) INFORMATION FOR SEQ ID NO:206:

- (i) SEQUENCE CHARACTERISTICS:
- (A) LENGTH: 37 amino acids
 - (B) TYPE: amino acid

- 255 -(D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 5 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Periodic Trp prt rI, Fig. 39 10 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:206: Gly His Ile Thr Thr His His Thr Asp Ala Val Leu Ser Met Ala His 15 5 Asn Lys Tyr Phe Arg Ser Val Leu Ala Ser Thr Ser Ala Asp His Thr 25 30 20 Val Lys Leu Trp Asp 35 (2) INFORMATION FOR SEQ ID NO:207: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 47 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 35 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: Periodic Trp prt rII, Fig. 39 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:207: Ile His Ser Asn Lys Asn Val Ser Ser Ser Glu Trp His Met Leu Asn 10 15 45

Gly Ser Ile Leu Leu Thr Gly Gly Tyr Asp Ser Arg Val Ala Leu Thr

WO 95/21252 PCT/US95/01210

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20 25 30

Asp Val Arg Ile Ser Asp Glu Ser Gln Met Ser Lys Tyr Trp Ser 35 40 45

5

- (2) INFORMATION FOR SEQ ID NO:208:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 amino acids
- 10 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 15 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 20 (C) INDIVIDUAL ISOLATE: PLAP rI, Fig. 40
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:208:
- Gly His Lys Asp Thr Val Cys Ser Leu Ser Ser Gly Lys Phe Gly Thr

Leu Leu Ser Gly Ser Trp Asp Thr Thr Ala Lys Val Trp Leu 20 25 30

- (2) INFORMATION FOR SEQ ID NO:209:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
- 35 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 40 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: PLAP rII, Fig. 40

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:209:

Gly His Thr Ala Ala Val Trp Ala Val Lys Ile Leu Pro Glu Gln Gly

1 5 10 15

5

Leu Met Leu Thr Gly Ser Ala Asp Lys Thr Ile Lys Leu Trp Lys
20 25 30

(2) INFORMATION FOR SEQ ID NO:210:

10

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

15

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 20 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: PLAP rIII, Fig. 40

25

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:210:
- Gly His Glu Asp Cys Val Arg Gly Leu Ala Ile Leu Ser Glu Thr Glu

 1 10 15

30

Phe Leu Ser Cys Ala Asn Asp Ala Ser Ile Arg Arg Trp Gln
20 25 30

(2) INFORMATION FOR SEQ ID NO:211:

35

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 45 (iv) ANTI-SENSE: NO

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(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: PLAP rIV, Fig. 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:211: 5 Gly His Thr Asn Tyr Ile Tyr Ser Ile Ser Val Phe Pro Asn Ser Lys 10 5 Asp Phe Val Thr Thr Ala Glu Asp Arg Ser Leu Arg Ile Trp Lys 10 25 20 (2) INFORMATION FOR SEQ ID NO:212: (i) SEQUENCE CHARACTERISTICS: 15 (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 20 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 25 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RETINOBLASTOMA BINDING PROTEIN -HUMAN. rI, Fig. 41 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:212: Gly His Gln Lys Glu Gly Tyr Gly Leu Ser Trp Asn Pro Asn Leu Ser 10 5 35 Gly His Leu Leu Ser Ala Ser Asp Asp His Thr Ile Cys Leu Trp Asp 25 20 (2) INFORMATION FOR SEQ ID NO:213: 40

(i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 32 amino acids
- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown 45

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| | (ii) MOLECULE TYPE: peptide |
|----|---|
| | (iii) HYPOTHETICAL: NO |
| 5 | (iv) ANTI-SENSE: NO |
| | <pre>(vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RETINOBLASTOMA BINDING PROTEIN -</pre> |
| 10 | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:213: |
| 15 | Gly His Thr Ala Val Val Glu Asp Val Ser Trp His Leu Leu His Gl |
| | Ser Leu Phe Gly Ser Val Ala Asp Asp Gln Lys Leu Met Ile Trp Asp 20 25 30 |
| 20 | (2) INFORMATION FOR SEQ ID NO:214: |
| 25 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 37 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| | (ii) MOLECULE TYPE: peptide |
| 30 | (iii) HYPOTHETICAL: NO |
| | (iv) ANTI-SENSE: NO |
| 35 | (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: RETINOBLASTOMA BINDING PROTEIN - HUMAN rIII, Fig. 41 |
| 40 | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:214: |
| | Ser His Ser Val Asp Ala His Thr Ala Glu Val Asn Cys Leu Ser Phe 1 5 10 15 |
| 45 | Asn Pro Tyr Ser Glu Phe Ile Leu Ala Thr Gly Ser Ala Asp Lys Thr 20 25 30 |

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Val Ala Leu Trp Asp 35

(2) INFORMATION FOR SEQ ID NO:215:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: RETINOBLASTOMA BINDING PROTEIN HUMAN rIV, Fig. 41

20

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:215:
- Ser His Lys Asp Glu Ile Phe Gln Val Gln Trp Ser Pro His Asn Glu

 25 1 5 10 15

Thr Ile Leu Ala Ser Ser Gly Thr Asp Arg Arg Leu Asn Val Trp Asp 20 25 30

30=

- (2) INFORMATION FOR SEQ ID NO:216:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids

- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- 40 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 45 (C) INDIVIDUAL ISOLATE: RETINOBLASTOMA BINDING PROTEIN HUMAN rV, Fig. 41

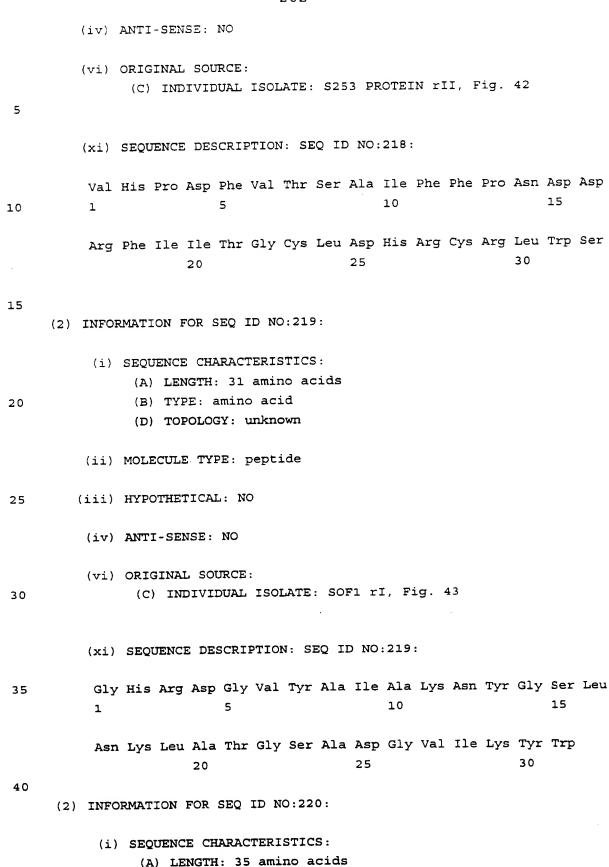
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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:216: Gly His Thr Ala Lys Ile Ser Asp Phe Ser Trp Asn Pro Asn Glu Pro 5 5 10 Trp Val Ile Cys Ser Val Ser Glu Asp Asn Ile Met Gln Val Trp Gln 20 25 10 (2) INFORMATION FOR SEQ ID NO:217: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids 15 (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 20 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: 25 (C) INDIVIDUAL ISOLATE: S253 PROTEIN rI, Fig. 42 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:217: 30 Glu His Ala Leu Asp Ile Leu Asp Ala Asn Trp Ser Lys Asn Gly Phe 5 10 15 Leu Ile Thr Ala Ser Met Asp Lys Thr Ala Lys Leu Trp His 20 25 30 35 (2) INFORMATION FOR SEQ ID NO:218: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids 40 (B) TYPE: amino acid (D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

(iii) HYPOTHETICAL: NO

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(B) TYPE: amino acid

(D) TOPOLOGY: unknown

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(ii) MOLECULE TYPE: peptide
         (iii) HYPOTHETICAL: NO
 5
         (iv) ANTI-SENSE: NO
          (vi) ORIGINAL SOURCE:
                (C) INDIVIDUAL ISOLATE: SOF1 rII, Fig. 43
10
          (xi) SEQUENCE DESCRIPTION: SEQ ID NO:220:
          Gly Leu Cys Val Thr Gln Pro Arg Phe His Asp Lys Lys Pro Asp Leu
                          5
                                               10
15
          Lys Ser Gln Asn Phe Met Leu Ser Cys Ser Asp Asp Lys Thr Val Lys
                      20
                                                               30
          Leu Trp Ser
20
                  35
     (2) INFORMATION FOR SEQ ID NO:221:
          (i) SEQUENCE CHARACTERISTICS:
25
               (A) LENGTH: 35 amino acids
               (B) TYPE: amino acid
               (D) TOPOLOGY: unknown
         (ii) MOLECULE TYPE: peptide
30
        (iii) HYPOTHETICAL: NO
         (iv) ANTI-SENSE: NO
35
         (vi) ORIGINAL SOURCE:
               (C) INDIVIDUAL ISOLATE: SOF1 rIII, Fig. 43
         (xi) SEQUENCE DESCRIPTION: SEQ ID NO:221:
40
         Gly Leu Ile Arg Thr Phe Asp Gly Glu Ser Ala Phe Gln Gly Ile Asp
         1
                          5
                                                                   15
         Ser His Arg Glu Asn Ser Thr Phe Ala Thr Gly Gly Ala Lys Ile His
45
                      20
                                          25
                                                               30
```

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Leu Trp Asp

35

(2) INFORMATION FOR SEQ ID NO:222:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 39 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: SOF1 rIV, Fig. 43

20

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:222:
- Gly His Ser Arg Glu Ile Tyr His Thr Lys Arg Met Gln His Val Phe 1 5 10 15

25

- Val Lys Tyr Ser Met Asp Ser Lys Tyr Ile Ile Ser Gly Ser Asp Asp 20 25 30
- Gly Asn Val Arg Leu Trp Arg

30 35

- (2) INFORMATION FOR SEQ ID NO:223:
 - (i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 31 amino acids

- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 45 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: STE4-YEAST rI, Fig. 44

(iv) ANTI-SENSE: NO

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(xi) SEQUENCE DESCRIPTION: SEQ ID NO:223: Gly His Asn Asn Lys Ile Ser Asp Phe Arg Trp Ser Arg Asp Ser Lys 5 10 Arg Ile Leu Ser Ala Ser Gln Asp Gly Phe Met Leu Ile Trp Asp 20 25 10 (2) INFORMATION FOR SEQ ID NO:224: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 30 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 15 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 20 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: STE4-YEAST rII, Fig. 44 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:224: Gly His Thr Cys Tyr Ile Ser Asp Ile Glu Phe Thr Asp Asn Ala His 30 5 10 1 15 Ile Leu Thr Ala Ser Gly Asp Met Thr Cys Ala Leu Trp Asp 20 30 35 (2) INFORMATION FOR SEQ ID NO:225: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 37 amino acids (B) TYPE: amino acid 40 (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO

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| į | (vri) | ORIGINAL | SOURCE: |
|---|--------|----------|---------|
| | | | |

- (C) INDIVIDUAL ISOLATE: STE4-YEAST rIII, Fig. 44
- 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:225:

Asp His Leu Gly Asp Val Leu Ala Leu Ala Ile Pro Glu Glu Pro Asn
1 5 10 15

Leu Glu Asn Ser Ser Asn Thr Phe Ala Ser Cys Gly Ser Asp Gly Tyr
20 25 30

Thr Tyr Ile Trp Asp 35

15

- (2) INFORMATION FOR SEQ ID NO:226:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
- 20 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 25 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 30 (C) INDIVIDUAL ISOLATE: STE4-YEAST rIV, Fig. 44
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:226:
- Leu Asp Asn Gln Gly Val Val Ser Leu Asp Phe Ser Ala Ser Gly Arg

 1 5 10 15

Leu Met Tyr Ser Cys Tyr Thr Asp Ile Gly Cys Val Val Trp Asp
20 25 30

- (2) INFORMATION FOR SEQ ID NO:227:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
- 45 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

- 267 -

| | | - 267 - |
|-----|-----------|--|
| | (ii) | MOLECULE TYPE: peptide |
| | (iii) | HYPOTHETICAL: NO |
| 5 | (iv) | ANTI-SENSE: NO |
| | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: STE4-YEAST rV, Fig. 44 |
| 10 | | |
| | | SEQUENCE DESCRIPTION: SEQ ID NO:227: |
| | | His Gly Gly Arg Val Thr Gly Val Arg Ser Ser Pro Asp Gly Leu |
| 15 | 1 | 5 10 15 |
| | Ala | Val Cys Thr Gly Ser Trp Asp Ser Thr Met Lys Ile Trp Ser 20 25 30 |
| 20 | (2) INFOR | RMATION FOR SEQ ID NO:228: |
| 25 | (i) | SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| 23 | (ii) | MOLECULE TYPE: peptide |
| | (iii) | HYPOTHETICAL: NO |
| 30 | (iv) | ANTI-SENSE: NO |
| | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TRNSCRPTION FCTR TIIF rI, Fig. 45 |
| 35 | | |
| | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:228: |
| 4.0 | Gly 1 | His Thr Gly Pro Val Tyr Arg Cys Ala Phe Ala Pro Glu Met Asn 5 10 15 |
| 40 | Leu | Leu Leu Ser Cys Ser Glu Asp Ser Thr Ile Arg Leu Trp Ser 20 25 30 |

(2) INFORMATION FOR SEQ ID NO:229:

45

(i) SEQUENCE CHARACTERISTICS:

| | | - 268 - |
|------|-----------------|---|
| | | (A) LENGTH: 31 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown |
| 5 | (ii) | MOLECULE TYPE: peptide |
| | (iii) | HYPOTHETICAL: NO |
| 10 | (iv) | ANTI-SENSE: NO |
| 10 | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TRNSCRPTION FCTR TIIF rII, Fig. 45 |
| -4-5 | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:229: |
| | Gly 1 | His Val Tyr Pro Val Trp Asp Val Arg Phe Ala Pro His Gly Tyr 5 10 15 |
| 20 | Tyr | Phe Val Ser Cys Ser Tyr Asp Lys Thr Ala Arg Leu Trp Ala 20 25 30 |
| | (2) INFO | RMATION FOR SEQ ID NO:230: |
| 25 | (i) | SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| 3.0 | (ii) | MOLECULE TYPE: peptide |
| | (iii) | HYPOTHETICAL: NO |
| 35 | (iv) | ANTI-SENSE: NO |
| | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TRNSCRPTION FCTR TIIF rIII, Fig. 4 |
| 40 | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:230: |
| | Gl _y | His Leu Ser Asp Val Asp Cys Val Gln Phe His Pro Asn Ser Asn 5 10 15 |
| 45 | The sec | r Val Ala Thr Gly Ser Ser Asp Arg Thr Val Arg Leu Trp Asp |

- (2) INFORMATION FOR SEQ ID NO:231:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
- 5 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: TRNSCRPTION FCTR TIIF rIV, Fig. 45
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:231:
- 20 Gly His Lys Gly Ser Val Ser Ser Leu Ala Phe Ser Ala Cys Gly Arg
 1 5 10 15
 - Tyr Leu Ala Ser Gly Ser Val Asp His Asn Ile Ile Ile Trp Asp
 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:232:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
- 30 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 35 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE
- 40 (C) INDIVIDUAL _ATE: TRNSCRPTION FCTR TIIF rV, Fig. 45
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:232:
- Arg His Thr Ser Thr Val Thr Thr Ile Thr Phe Ser Arg Asp Gly Thr

 1 5 10 15

- 270 -

Val Leu Ala Ala Ala Gly Leu Asp Asn Asn Leu Thr Leu Trp Asp 20 25 30

(2) INFORMATION FOR SEQ ID NO:233:

5

- (i) SEOUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: TUP1 rI, Fig. 46

20

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:233:
- Ser Ser Asp Leu Tyr Ile Arg Ser Val Cys Phe Ser Pro Asp Gly Lys

 1 10 15

25

- Phe Leu Ala Thr Gly Ala Glu Asp Arg Leu Ile Arg Ile Trp Asp 20 25 30
- (2) INFORMATION FOR SEQ ID NO:234:

30

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

35

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 40 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: TUP1 rII, Fig. 46

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:234:

25

45

- 271 -

Gly His Glu Gln Asp Ile Tyr Ser Leu Asp Tyr Phe Pro Ser Gly Asp

1 10 15

Lys Leu Val Ser Gly Ser Gly Asp Arg Thr Val Arg Ile Trp Asp
5 20 25 30

- (2) INFORMATION FOR SEQ ID NO:235:
 - (i) SEQUENCE CHARACTERISTICS:

10 (A) LENGTH: 31 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
- 20 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: TUP1 rIII, Fig. 46
 - (xi) SEQUENCE DESCRIPTION: SEO ID NO:235:

Ile Glu Asp Gly Val Thr Thr Val Ala Val Ser Pro Gly Asp Gly Lys

1 5 10 15

Tyr Ile Ala Ala Gly Ser Leu Asp Arg Ala Val Arg Val Trp Asp 30 20 25 30

- (2) INFORMATION FOR SEQ ID NO:236:
- 35 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 40 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
- (vi) ORIGINAL SOURCE:

- 272 -

(C) INDIVIDUAL ISOLATE: TUP1 rIV, Fig. 46

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:236:

5

Gly His Lys Asp Ser Val Tyr Ser Val Val Phe Thr Arg Asp Gly Gln

1 5 10 15

Ser Val Val Ser Gly Ser Leu Asp Arg Ser Val Lys Leu Trp Asn 20 25 30

- (2) INFORMATION FOR SEQ ID NO:237:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 31 amino acids

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

(ii) MOLECULE TYPE: peptide

20

15

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 25 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: TUP1 rV, Fig. 46
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:237:

30

Gly His Lys Asp Phe Val Leu Ser Val Ala Thr Thr Gln Asn Asp Glu

1 10 15

Tyr Ile Leu Ser Gly Ser Lys Asp Arg Gly Val Leu Phe Trp Asp 20 25 30

- (2) INFORMATION FOR SEQ ID NO:238:
 - (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 22 amino acids

- (B) TYPE: amino acid
- (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide

45

40

(iii) HYPOTHETICAL: NO

- 273 -

| | 2,3 | |
|-----|---|---|
| | (iv) ANTI-SENSE: NO | |
| 5 . | (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG rI, Fig. 47 | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:238: | |
| 10 | Asp Phe Ser Asp Asp Cys Arg Ile Ala Ala Ala Gly Phe Gln Asp Ser | כ |
| | Tyr Ile Lys Ile Trp Ser 20 | |
| 15 | (2) INFORMATION FOR SEQ ID NO:239: | |
| 20 | (i) SEQUENCE CHARACTERISTICS:(A) LENGTH: 31 amino acids(B) TYPE: amino acid(D) TOPOLOGY: unknown | |
| | (ii) MOLECULE TYPE: peptide | |
| 25 | (iii) HYPOTHETICAL: NO | |
| | (iv) ANTI-SENSE: NO | |
| 30 | (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG rII, Fig. 47 | |
| | (xi) SEQUENCE DESCRIPTION: SEQ ID NO:239: | |
| 35 | Gly His Ser Gly Thr Val Tyr Ser Thr Ser Phe Ser Pro Asp Asn Lys 1 5 10 15 | |
| | Tyr Leu Leu Ser Gly Ser Glu Asp Lys Thr Val Arg Leu Trp Ser 20 25 30 | |
| 10 | (2) INFORMATION FOR SEQ ID NO:240: | |

(i) SEQUENCE CHARACTERISTICS:

(B) TYPE: amino acid

(D) TOPOLOGY: unknown

45

(A) LENGTH: 31 amino acids

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| | (ii) | MOLECULE TYPE: peptide |
|-----|----------------------|--|
| | (iii) | HYPOTHETICAL: NO |
| 5 | (iv) | ANTI-SENSE: NO |
| | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG rIII, Fig. 47 |
| 10 | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:240: |
| *** | Gly 1 | His Asn His Pro Val Trp Asp Val Ser Phe Ser Pro Leu Gly His 5 10 15 |
| 15 | Tyr | Phe Ala Thr Ala Ser His Asp Gln Thr Ala Arg Leu Trp Ser 20 25 30 |
| 20 | (2) INFO | RMATION FOR SEQ ID NO:241: |
| 25 | (i) | SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| | (ii) | MOLECULE TYPE: peptide |
| 30 | (iìi) | HYPOTHETICAL: NO |
| | (iv) | ANTI-SENSE: NO |
| | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG rIV, Fig. 47 |
| 35 | | |
| | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:241: |
| 40 | Gl _y 1 | y His Leu Asn Asp Val Asp Cys Val Ser Phe His Pro Asn Gly Cys 5 10 15 |
| | Тy | r Val Phe Thr Gly Ser Ser Asp Lys Thr Cys Arg Met Trp Asp 20 25 30 |

45 (2) INFORMATION FOR SEQ ID NO:242:

- 275 -

(i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 31 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 5 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 10 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG rV, Fig. 47 15 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:242: Gly His Thr Ala Pro Val Ile Ser Ile Ala Val Cys Pro Asp Gly Arg 5 20 Trp Leu Ser Thr Gly Ser Glu Asp Gly Ile Ile Asn Val Trp Asp 25 (2) INFORMATION FOR SEO ID NO:243: 25 (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 32 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown 30 (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO 35 (iv) ANTI-SENSE: NO (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: TUP1 HOMOLOG rVI, Fig. 47 40 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:243: Gly His Gly Lys Asn Ala Ile Tyr Ser Leu Ser Tyr Ser Lys Glu Gly 10 45

Asn Val Leu Ile Ser Gly Gly Ala Asp His Thr Val Arg Val Trp Asp

30

(2) INFORMATION FOR SEQ ID NO:244:

20

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: YCU7 rI, Fig. 48

20

- (xi) SEQUENCE DESCRIPTION: SEQ ID NO:244:
- Gly His Phe Asp Ser Thr Asn Ser Leu Ala Tyr Ser Pro Asp Gly Ser

1 5 10 15

25

Arg Val Val Thr Ala Ser Glu Asp Gly Lys Ile Lys Val Trp Asp 20 25 30

(2) INFORMATION FOR SEQ ID NO:245:

3.0

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

35

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 40 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: YCU7 rII, Fig. 48

45

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:245:

- 277 -

Glu His Thr Ser Ser Val Thr Ala Val Gln Phe Ala Lys Arg Gly Gln

1 10 15

Val Met Phe Ser Ser Leu Asp Gly Thr Val Arg Ala Trp Asp
20 25 30

- (2) INFORMATION FOR SEQ ID NO:246:
- 10 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 30 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 15 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

20

- (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: YCU7 rIII, Fig. 48
- 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:246:

Arg Ile Gln Phe Asn Cys Leu Ala Val Asp Pro Ser Gly Glu Val Val 1 5 10 15

- Cys Ala Gly Ser Leu Asp Asn Phe Asp Ile His Val Trp Ser 20 25 30
 - (2) INFORMATION FOR SEQ ID NO:247:
- 35 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 40 (ii) MOLECULE TYPE: peptide
 - (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO

45

(vi) ORIGINAL SOURCE:

- 278 -

(C) INDIVIDUAL ISOLATE: YCU7 rIV, Fig. 48

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:247:

5

Gly His Glu Gly Pro Val Ser Cys Leu Ser Phe Ser Gln Glu Asn Ser

1 10 15

Val Leu Ala Ser Ala Ser Trp Asp Lys Thr Ile Arg Ile Trp Ser

20 25 30

- (2) INFORMATION FOR SEQ ID NO:248:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide

20

15

- (iii) HYPOTHETICAL: NO
- (iv) ANTI-SENSE: NO
- 25 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rI, Fig. 49
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:248:

30

Gly His Gly Ser Thr Ile Leu Cys Ser Ala Phe Ala Pro His Thr Ser

Ser Arg Met Val Thr Gly Ala Gly Asp Asn Thr Ala Arg Ile Trp Asp 20 25 30

- (2) INFORMATION FOR SEQ ID NO:249:
- 40 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- 45 (ii) MOLECULE TYPE: peptide

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| | | 2.73 |
|----|----------|--|
| | (iii) | HYPOTHETICAL: NO |
| | (iv) | ANTI-SENSE: NO |
| 5 | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rII, Fig. 49 |
| 10 | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:249: |
| 10 | Gly 1 | His Tyr Asn Trp Val Leu Cys Val Ser Trp Ser Pro Asp Gly Gl |
| 15 | Val | Ile Ala Thr Gly Ser Met Asp Asn Thr Ile Arg Leu Trp Asp 20 25 30 |
| | (2) INFO | RMATION FOR SEQ ID NO:250: |
| 20 | (i) | SEQUENCE CHARACTERISTICS: (A) LENGTH: 38 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown |
| 25 | (ii) | MOLECULE TYPE: peptide |
| | (iii) | HYPOTHETICAL: NO |
| | (iv) | ANTI-SENSE: NO |
| 30 | (vi) | ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rIII, Fig. 49 |
| | (xi) | SEQUENCE DESCRIPTION: SEQ ID NO:250: |
| 35 | Gly 1 | His Ser Lys Trp Ile Thr Ser Leu Ser Trp Glu Pro Ile His Leu 5 10 15 |
| 40 | Val | Lys Pro Gly Ser Lys Pro Arg Leu Ala Ser Ser Ser Lys Asp Gly 20 25 30 |
| | Thr | Ile Lys Ile Trp Asp 35 |

(2) INFORMATION FOR SEQ ID NO:251:

45

(i) SEQUENCE CHARACTERISTICS:

- 280 -(A) LENGTH: 30 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 10 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rIV, Fig. 49 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:251: 15. Gly His Thr Asn Ser Val Ser Cys Val Lys Trp Gly Gly Gln Gly Leu 10 5 Leu Tyr Ser Gly Ser His Asp Arg Thr Val Arg Val Trp Asp 20 20 (2) INFORMATION FOR SEQ ID NO:252: (i) SEQUENCE CHARACTERISTICS: 25 (A) LENGTH: 26 amino acids (B) TYPE: amino acid (D) TOPOLOGY: unknown (ii) MOLECULE TYPE: peptide 30 (iii) HYPOTHETICAL: NO (iv) ANTI-SENSE: NO 35 (vi) ORIGINAL SOURCE: (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rV, Fig. 49 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:252: 40 Lys Ile Cys Lys Lys Asn Gly Asn Ser Glu Glu Met Met Val Thr Ala 5 15

Ser Asp Asp Tyr Thr Met Phe Leu Trp Asn 20 25

- (2) INFORMATION FOR SEO ID NO:253:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 25 amino acids
- 5 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rVI, Fig. 49
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:253:
- Asn His Val Ala Phe Ser Pro Asp Gly Arg Tyr Ile Val Ser Ala Ser

 1 5 10 15

Phe Asp Asn Ser Ile Lys Leu Trp Asp 20 25

- (2) INFORMATION FOR SEQ ID NO:254:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
- 30 (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 35 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 40 (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rVII, Fig. 49
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:254:
- Gly His Ile Ala Ser Val Tyr Gln Val Ala Trp Ser Ser Asp Cys Arg

 1 5 10 15

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Leu Leu Val Ser Cys Ser Lys Asp Thr Thr Leu Lys Val Trp Asp 20 25 30

(2) INFORMATION FOR SEQ ID NO:255:

5

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 35 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown

10

- (ii) MOLECULE TYPE: peptide
- (iii) HYPOTHETICAL: NO
- 15 (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: YCW2 PROTEIN rVIII, Fig. 49
 - 20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO:255:

Ser Val Asp Leu Pro Gly Ile Lys Thr Lys Leu Tyr Val Asp Trp Ser 1 5 10 15

Val Asp Gly Lys Arg Val Cys Ser Gly Gly Lys Asp Lys Met Val Arg 20 25 30

Leu Trp Thr

- (2) INFORMATION FOR SEQ ID NO:256:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 29 amino acids
- (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: YKL525 rI, Fig. 50
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:256:
- Leu His Leu Tyr Ala Pro Val Phe Tyr Ser Asp Val Phe Arg Val Phe
 1 5 10 15

Met Glu His Ala Leu Asp Ile Leu Asp Ala Asn Trp Ser 20 25

| (2) INFORMATION | FOR | SEQ | ID | NO:257 |
|-----------------|-----|-----|----|--------|
|-----------------|-----|-----|----|--------|

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
- (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: YKL525 rII, Fig. 50
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:257:
- Val His Pro Asp Phe Val Thr Ser Ala Ile Phe Phe Pro Asn Asp Asp

 1 5 10 15
 - Arg Phe Ile Ile Thr Gly Cys Leu Asp His Arg Cys Arg Leu Trp Ser 20 25 30

- (2) INFORMATION FOR SEQ ID NO:258:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: yrb 1410 yeast rI, Fig. 51
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:258:
- 20 Gly His Asn His Pro Val Trp Asp Val Ser Phe Ser Pro Leu Gly His 1 5 10 15
 - Tyr Phe Ala Thr Ala Ser His Asp Gln Thr Ala Arg Leu Trp Ser 20 25 30

- 286 -

| (2) | INFORMATION | FOR | SEQ | ID | NO:259: |
|-----|-------------|-----|-----|----|---------|
|-----|-------------|-----|-----|----|---------|

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
- (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15. (C) INDIVIDUAL ISOLATE: yrb 1410 yeast rII, Fig. 51
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:259:
- Gly His Leu Asn Asp Val Asp Cys Val Ser Phe His Pro Asn Gly Cys

 1 5 10 15

Tyr Val Phe Thr Gly Ser Ser Asp Lys Thr Cys Arg Met Trp Asp 20 25 30

- (2) INFORMATION FOR SEQ ID NO:260:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 31 amino acids
- (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: yrb 1410 yeast rIII, Fig. 51
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:260:
- 20 Gly His Thr Ala Pro Val Ile Ser Ile Ala Val Cys Pro Asp Gly Arg
 1 5 10 15
 - Trp Leu Ser Thr Gly Ser Glu Asp Gly Ile Ile Asn Val Trp Asp 20 25 30

25

- 288 -

| (2) | INFORMATION | FOR | SEQ | ID | NO:261: |
|-----|-------------|-----|-----|----|---------|
|-----|-------------|-----|-----|----|---------|

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 32 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
 - , = ,
- (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: yrb 1410 yeast rIV, Fig. 51
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:261:
- 20 Gly His Gly Lys Asn Ala Ile Tyr Ser Leu Ser Tyr Ser Lys Glu Gly
 1 5 10 15
 - Asn Val Leu Ile Ser Gly Gly Ala Asp His Thr Val Arg Val Trp Asp 20 25 30

25

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| (2) INFORMATION FOR SEQ ID NO: | :262: |
|--------------------------------|-------|
|--------------------------------|-------|

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 34 amino acids
 - (B) TYPE: amino acid
 - (D) TOPOLOGY: unknown
- (ii) MOLECULE TYPE: peptide
- 10 (iii) HYPOTHETICAL: NO
 - (iv) ANTI-SENSE: NO
 - (vi) ORIGINAL SOURCE:
- 15 (C) INDIVIDUAL ISOLATE: WD40 Consensus Sequence
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:262:
- Gly His Ser Ala Ala Leu Ala Leu Ala Leu Ser Pro Asp Ala Ala 20 1 5 10 15
 - Ala Ala Ala Leu Ala Ser Gly Ala Arg Asp Ala Thr Leu Arg Leu Trp
 20 25 30
- 25 Asp Leu

(2) INFORMATION FOR SEQ ID NO:263:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 5 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
- (ii) MOLECULE TYPE: peptide

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- (iii) HYPOTHETICAL: YES
- (iv) ANTI-SENSE: NO
- 15 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: WRTAA peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:263:
- 20 Trp Arg Thr Ala Ala

- (2) INFORMATION FOR SEQ ID NO:264:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 5 amino acids
 - (B) TYPE: amino acid
 - (C) STRANDEDNESS: single
 - (D) TOPOLOGY: linear
 - (ii) MOLECULE TYPE: peptide
- 10

- (iii) HYPOTHETICAL: YES
- (iv) ANTI-SENSE: NO
- 15 (vi) ORIGINAL SOURCE:
 - (C) INDIVIDUAL ISOLATE: WRTAV peptide
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO:264:
- 20 Trp Arg Thr Ala Val
 - 1 5

- 292 -

(2) INFORMATION FOR SEQ ID NO:265:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 4 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: peptide

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(iii) HYPOTHETICAL: YES

(iv) ANTI-SENSE: NO

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(vi) ORIGINAL SOURCE:

(C) INDIVIDUAL ISOLATE: WRTA peptide

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:265:

20 Trp Arg Thr Ala

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Claims

1. A polypeptide composition effective to alter the activity of a first protein, wherein the first protein interacts with a second protein, and the second protein contains at least one WD-40 region,

said polypeptide having between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in the WD-40 region of the second protein.

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- 2. The composition of claim 1, wherein said polypeptide inhibits interactions between the first protein and the second protein; and/or wherein said polypeptide is an agonist of the activity of the first protein; and/or wherein said polypeptide is an antagonist of the activity of the first protein.
- 3. The composition of claim 1 or 2, wherein said WD-40 region has an amino acid sequence derived from the group consisting of SEQ ID NO:76-261.

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- 4. The composition of claim 3, wherein said WD-40 region has an amino acid sequence selected from the group consisting of SEQ ID NO:76-261.
- 5. The polypeptide composition of claim 1 wherein said polypeptide is coupled to a solid support.
 - 6. A method to bind selectively said first protein which method comprises contacting a sample putatively containing said first protein with the polypeptide composition of claim 5; and

removing any unbound components of the sample from said composition.

7. A method to assess the interaction of a first protein
with a polypeptide having a sequence the same as a sequence of the same
length contained in a WD-40 region of a second protein, which method
comprises

contacting a sample containing said first protein with a polypeptide composition wherein the polypeptide has between 4 and 50 amino acids whose sequence is the same as the sequence of the same length in the WD-40 region of the second protein, and observing any interaction of the first protein with said polypeptide composition.

8. A method to assess the ability of a candidate compound to bind a first protein which method comprises contacting said first protein with a polypeptide composition which binds said first protein,

wherein the polypeptide of said composition has between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in a WD-40 region of a second protein which interacts with said first protein, in the presence and absence of said candidate compound; and

measuring the binding of said polypeptide in the presence and in the absence of said candidate,

wherein decreased binding of the polypeptide in the presence as opposed to the absence of said candidate indicates that said candidate binds to said first protein.

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9. A method to alter the activity of a first protein that interacts with a second protein, where the second protein contains at least one WD-40 region, said method comprising

selecting a polypeptide having between 4 and 50 amino acids
whose sequence is the same as a sequence of the same length in the WD-40
region in the second protein, and

contacting said polypeptide with said first protein under conditions which allow the formation of a complex between the polypeptide and the first protein, where said interaction is effective to alter the activity of the first protein.

- 10. The method of claim 9, wherein said contacting is effective to inhibit the interaction between said first and second proteins; and/or wherein said contacting is effective to stimulate the activity of said first protein; and/or wherein said contacting is effective to inhibit the activity of said first protein.
- 11. The method of any of claims 5-10, wherein said polypeptide is derived from the group consisting of SEQ ID NO:76-261.
 30.331
 - 12. The method of claim 11, wherein said polypeptide is selected from the group consisting of SEQ ID NO:76-261.
- 13. A composition of DNA molecules which consists of DNA molecules having a nucleotide sequence encoding the polypeptide of any of claims 1-4.
- 14. A DNA molecule which comprises an expression system for the production of the polypeptide of any of claims 1-4 which expression system comprises a nucleotide sequence encoding said polypeptide operably linked to control sequences capable of effecting the expression of said encoding nucleotide sequence.
- 15. Recombinant host cells modified to contain the 45 expression system of claim 14.

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16. A method to produce a polypeptide having between 4 and 50 amino acids whose sequence is the same as the sequence of the same length in a WD-40 region of a second protein which interacts with a first protein, which method comprises culturing the cells of claim 15 under conditions wherein said nucleotide sequence is expressed to produce said polypeptide; and

optionally recovering said polypeptide from the culture.

17. A polypeptide composition effective to alter the activity of a protein kinase C, where the protein kinase C interacts with a second protein, and the second protein contains at least one WD-40 region,

said polypeptide having between 4 and 50 amino whose sequence is the same as a sequence of the same length in the WD-40 region of the second protein.

- 18. The composition of claim 17, wherein said second protein is a receptor for activated protein kinase C.
- 19. The composition of claim 18, where said second protein has the sequence represented by SEQ ID NO:27.
- 20. The composition of claim 17, wherein said polypeptide is an agonist of the activity of protein kinase C; and/or wherein said polypeptide is an antagonist of the activity of protein kinase C; and/or wherein said polypeptide inhibits interactions between protein kinase C and the second protein.
- 21. The composition of claim 20 wherein said polypeptide 30 has the sequence represented by SEQ ID NO:7, SEQ ID NO:4 or SEQ ID NO:2.
 - 22. The composition of claim 17, wherein said WD-40 region has an amino acid sequence derived from the group consisting of SEQ ID NO:69-75.
 - 23. The composition of claim 22, wherein said WD-40 region has an amino acid sequence selected from the group consisting of SEQ ID NO:69-75.
- 24. The polypeptide composition of claim 17 wherein said polypeptide is coupled to a solid support.
- 25. A method to bind selectively protein kinase C which method comprises contacting a sample putatively containing protein kinase C with the polypeptide composition of claim 24; and

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removing any unbound components of the sample from said composition.

26. A method to assess the interaction of protein kinase C with a polypeptide having a sequence the same as a sequence of the same length contained in the WD-40 region of a second protein, which method comprises

contacting a sample containing said protein kinase C with a polypeptide composition wherein the polypeptide has between 4 and 50 amino acids whose sequence is the same as the sequence of the same length in the WD-40 region of the second protein, and observing any interaction of the protein kinase C with said polypeptide composition.

27. A method to assess the ability of a candidate compound to bind protein kinase C which method comprises contacting said protein kinase C with a polypeptide composition which binds said protein kinase C, wherein the polypeptide of said composition has between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in a WD-40 region of a second protein which interacts with said protein kinase C, in the presence and absence of said candidate compound; and

measuring the binding of said polypeptide in the presence and in the absence of said candidate,

wherein decreased binding of the polypeptide in the presence as opposed to the absence of said candidate indicates that said candidate binds to said protein kinase C.

- 28. A method to alter the activity of protein kinase C that interacts with a second protein, where the second protein contains at least one WD-40 region, comprising
- selecting a polypeptide having between 4 and 50 amino acids whose sequence is the same as a sequence of the same length in the WD-40 region in the second protein, and

contacting said polypeptide with said protein kinase C under conditions which allow the formation of a complex between the polypeptide and the protein kinase C, where said interaction alters the activity of said protein kinase C.

29. The method of claim 28, wherein said contacting is effective to inhibit the interaction between said protein kinase C and said second protein; and/or wherein said contacting is effective to stimulate the activity of said protein kinase C; and/or wherein said contacting is effective to inhibit the activity of said protein kinase C.

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- 30. The method of claim 29, wherein said polypeptide has an amino acid sequence represented by SEQ ID NO:2, SEQ ID NO:4 or SEQ ID NO:7.
- 5 31. The method of claim 28, wherein said polypeptide is derived from the group consisting of SEQ ID NO:69-75.
 - 32. The method of claim 31, wherein said polypeptide is selected from the group consisting of SEQ ID NO:69-75.
- 33. A composition of DNA molecules which consists of DNA molecules having a nucleotide sequence of encoding the polypeptide of any of claims 17-23.
- 15 34. A DNA molecule which comprises an expression system for the production of the polypeptide of any of claims 17-23 which expression system comprises a nucleotide sequence encoding said polypeptide operably linked to control sequences capable of effecting the expression of said encoding nucleotide sequence.
 - 35. Recombinant host cells modified to contain the expression system of claim 34.
- 36. A method to produce a polypeptide having between 4 and 50 amino acids whose sequence is the same as the sequence of the same length in a WD-40 region of a second protein which interacts with protein kinase C, which method comprises culturing the cells of claim 35 under conditions wherein said nucleotide sequence is expressed to produce said polypeptide; and
- optionally recovering said polypeptide from the culture.

CAGACTCTTA GAAATAAACT CAAGGATGTG GAGTCATTCA GACCAACCAC GCACCTTTAC CATGGTAGAT GTGTACCTCT CTTGGTGCGT CTGGGTCCCG AGACAAGACC CCTCTGTGCT GCAGTTCCCG **AACCCTACGC** CGTCTCCTGC CTACTGGCT(GGCACGAGGG GTCGCGGTGG CAGCCGTGCG GTGCTTGGCT CCCTAAGCTA TCCGGTGCCA TGTTAGCGAT GACCAGGGAT CCGAGCAAAT GACCCTTCGI CAGATGGATC GCCCCAACCG GCAAGCTAAA ATACCGACAA TCCAGGATGA ATGAAGGCAA AGGGCAAGAT AGCCACCCCA CCTGGGATGG **ACCCTATCAT** TCGGCCACAC CCACCACTCC ACCATCATCA TGTGGAAGCT ACTCCCACTT **AAGTTTATGA** TGGGACTTGG AGCAAGGCAG **AAGTACACTG** AACAGCAGCA TGGGATCTCA TTGTGCTTCA TTTGCTGGCT CTGGCTAACT GCAGCCATTCA AGACGATTTG CAGATTGTCT ACTGTCTCTC **ACACAGATCG** CTTCGAGGTC CTCTCAGGCT GGCTTTCTGA AAAAAAAAA AAAAAAAAA AAAAA GTATGGCAGG TGACTATTGG TACCCGCTAA GAACACAGTG GGCTATGCTG CCAGACTCTG CTTCTCCCCG TATCAAGATC CAGCACCAGC CACTACCACG TGACAACCGG GGGTGTCTGC CATCAATGCC TCGAGACAAG GGTGTGGAAT CGCAACATCT CCAGTTTGCC **ACAACGTGCT** TGGATGGGTT CTGGCCCCAG CTGCTGATGG **AAGAAGTTAT** CCTCTGATGG CTTGTGTCCG AGCTGGTCAA AGGATGGCCA GTGGAGACAT rgrcggcg1C ACGGCATACC TCACAACGGG CTTTCTCCTC CTGGCTATCT AGGGCCATAA **GGAATACTCT TGCGGCGACT** TCTGGAGGCA **ACATTAGATG** TGTGCTGCCA GAACTGAAGC TGGCTTGGT CTGAGCGTGG GGATGGGACA **ATTGGCCACA** TCCTTGTCGC **GGGACCCTCA** GACATGATCC CTCTGGGATC ATTAAGTTAT GAATGGGTGT GAGACCAACT GTTGTCATCT **661** 841 361 421 481 541 601 721 241 301

Fig. 1A

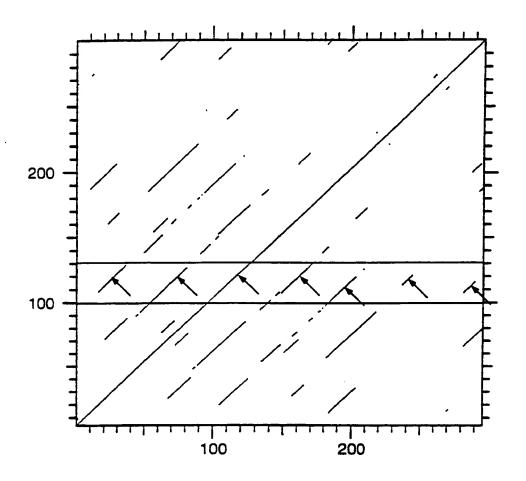


Fig. 1B

RepeatVII

Repeat III Repeat IV

RepeatV

Repeat II

Repeat I

RepeatVI NEGKHLYTLDGGDII NALCESPNRYWLCAATGPSIKIWDLEGKIIVDE (269) MTEQMTLRGTLKGHNGWVYQ IATTPQFPDMILSASRDKTIIMWKLTRDETN(51) LKQEVISTSSKAEP<u>POCTSLA</u>WBADGQTLFAGYTDNLVRVWQVTIGTR(317) TGTTTRRFVGHTKDVL SVAESSDNRQIVSGSRDKTIKLWNTLG(136) VCKYTVQDESHSEW<u>VSCVRFS</u>PNSSNPIIV8CGWDKLVKVWNLA(180) DVVI SSDGQFALSGSWDGTLRLWDLT(93) NCKLKTNHIGHTGYLN TVTV8PDGSLCASGGKDGQAMLWDL (221) YGI PORALR**GHS**H**EVS**

Rat RACKI

GHS--V---V--SSD---ILSG--D-TIKLW-L GH --- I --- SVA --- DG -- LVTGS - D -- C - IWDL

Consensus sequence of repeats:

Rat RACK1 Human GB2

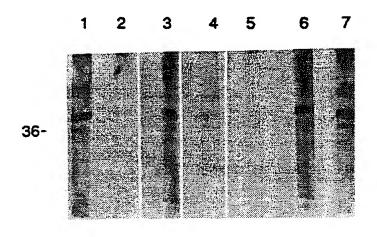
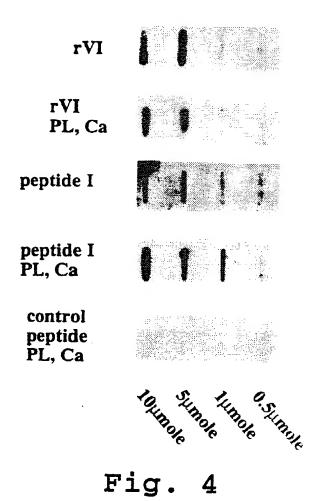
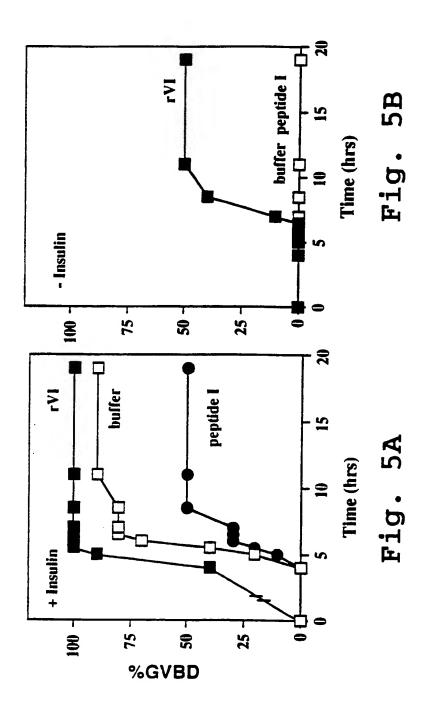


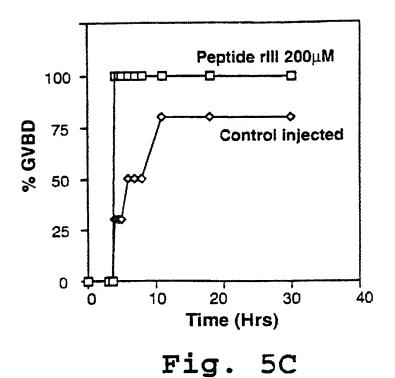
Fig. 2



Fig. 3







pc pcpc pc

bPKC

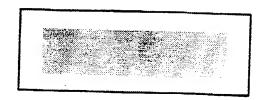
1 2 3 4 5 6 7 8

Peptide - rVI - I
Insulin - + +

Fig. 6

| 80- 78- | | | | | | • | *************************************** | • | |
|--------------------------|----|------|------|-----|-----|-----|---|-----|-----|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
| Arg-c | • | + | + | + | + | + | + | + | + |
| PS(mg) | - | 50 | 50 | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 | 2.5 |
| DG (0.8 μg) | - | + | - | • | • | - | - | - | - |
| Ca (mM) | - | 1000 | 1000 | 50 | 50 | 50 | 50 | 50 | 50 |
| Peptide (10mM) | - | - | - | • | rVI | rVI | rVI | С | I |
| Time of incubation (min) | 30 | 30 | 30 | 30 | 5 | 15 | 30 | 30 | 30 |

Fig. 7



| TIC TO CLO | 1 | 2 | 3 | 4 | 5 | 6 | |
|---|---|----|---|-----|---|---|--|
| PS/DG/Ca | + | • | • | • | - | - | |
| EGTA | - | + | • | - | - | • | |
| Anti-pseudo- substrate antibodies | - | - | + | - | - | - | |
| peptides (10mM) | • | ₩. | • | rVI | I | C | |

Fig. 8

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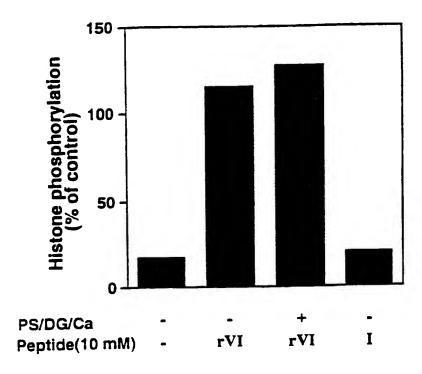


Fig. 9

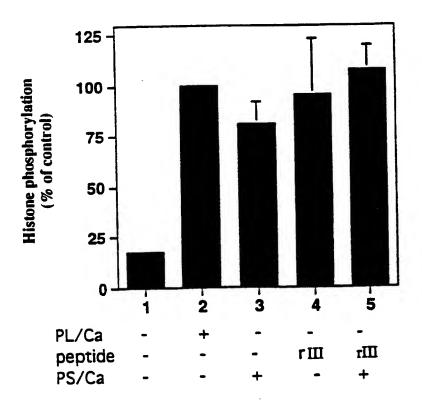


Fig. 10

SUBSTITUTE SHEET (RULE 26)

Fig. 11

Human 56 kDa protein (PWP homolog)

1 mnrsrqvtcv awvrcgvake tpdkvelske evkrliaeak eklqeegggs
51 deeetgspse dgmqsartqa rprepledgd peddrtlddd elaeydldky
101 deegdpdaet lgesllgltv ygsndqdpyv tlkdteqyer edflikpsdn
151 livcgraeqd qcnlevhvyn qeedsfyvhh dillsaypls vewlnfdpsp
201 ddstgnyiav gnmtpvievw dldivdslep vftlgsklsk kkkkkgkkss

251 saeghtdavldlswnkl irnvldsasadntvilwdmslgk

291 paaslavhtd kvqtlqfhpf eaqtlisgsy dksvalydcr

331 spdeshrmwr fsgqiervtw 351 nhfspchfla stddgfvynl darsdkpift

381 lna<u>h</u>ndeisgldlssqi kgclvtasa<u>d</u>kyvki<u>wd</u>ilgdrp

421 slvhsrdmkmgvlfcssccpdlpfiyafggqkegl rvwdi

461 styssyneaf grrerlylgs armssisgpf gsrssdtpme

501 s

AAC-RICH protein

| 1 51 101 | pggfahlaga qatqahlatq dsknldlasr | pggfqhlqqq qqqqqqqq qqqqqqqtq vqqlhnqlhq qhnqqiqqqa qatqqhlqtq qylqsqihqq sqqsqlsnnl nsnskestni pktntqytnf dsknldlasr yfsecstkdfi | qqqqqqqtq sqqsqlsnnl i | vqqlhnqlhq nsnskestni | pggfqhlqqq qqqqqqqq qqqqqqqtq vqqlhnqlhq qhnqqiqqqa qatqqhlqtq qylqsqihqq sqqsqlsnnl nsnskestni pktntqytnf dsknldlasr yfsecstkdfi | |
|----------------|--|---|------------------------------|--------------------------|---|--|
| | | | | | | |

| <u>gn</u> kkkstsvawnangtkia s _s gs <u>d</u> givrv <u>wn</u> fd | | elk gh dgsiekiswspknndlla s <mark>ngtd</mark> kvik iwdy kigkcigtvstnsenid | ge <u>e</u> lnqvg wd nngdlilmansmgnieayk | laagsa <u>d</u> sivs lwdi edm |
|---|-----------------------------|---|---|--|
| stsvawnangtkia | sknnniketi | ;iekiswspknndlla | vrwspdgdhla idlptiktlkiykfn | : iycmefdptg ky |
| gnkk | plgnsnnnnsnntss nsknnniketi | elk gh dg | vrwspdgdhla | 301 lpkstthvkhlktly gh tas iycmefdptg kylaagsagsivs lwdi edm |
| 122 | 155 | 182 | 235 | 301 |

351 mcvktfikst fpcrsvsfsf dggfiaassf estieifhie 411 ssqpihtiecgvsslmwhptlpllayapesinennkdpsi rvfgyhs

Fig. 12

BETA TRCP

1 megfscslqp ptaseredcn rdepprkiit ekntlrqtklangtssmivp 51 kqrklsanye kekelcvkyf eqwsecdqve fvehlisrmchyqhghinty 101 lkpmlqrdfi talpargldh iaenilsyld akslcsaelv ckewyrvtsd 151 gmlwkklier mvrtdslwrg laerrgwgqy lfknkppdgk tppnsfyral 201 ypkiiqdiet iesnwrcgr

| 220 | hslqr <u>ih</u> cr | se tskgvyclqyddq | kivsglr d n <u>tikiwd</u> kn tleckrv |
|-----|-----------------------|----------------------|--|
| 268 | lm <u>ah</u> tg | svlclqy dei | viitgs <u>d</u> s <u>tvrvwdv</u> ntgem |
| 305 | lntl <u>ih</u> hce | pvlhlrfnngmmvtcs | <u>d</u> r <u>s</u> ia <u>vwdm</u> asatditlrrv |
| 351 | lv gh raa | vnv vdfddkyivs | asg <u>d</u> r <u>tikvwn</u> tstcefvrt |
| 391 | ln gh krg | laclqyrdrlvvs | gss <u>d</u> n <u>tirlwdi</u> ecga |
| 427 | clrv le <u>gh</u> eel | vrc irfdnkrivs | gay <u>dg</u> k <u>ikvwdl</u> vaaldprapagt |
| 475 | lclrtlve <u>h</u> sgr | vfrl qfdefqi | vssshd d t i l <u>iwdflndpgla</u> |
| | | | |

Fig. 13

beta-prime-cop

vks vdlhptepwmlaslyngsvcvwnhetqtlv 51 ktfevcdlpv raakfvarkn wvvtgaddmqirvfnyntle

| 91 | rvhmfe <u>ah</u> sdy | irciavhptqp | • | filtssd <u>d</u> mli <u>klwdw</u> dkkwscsq |
|-----|----------------------|--------------|-------|--|
| 137 | vfe gh thy | vmqivinpkdnr | ıqfa: | s asl <u>d</u> r <u>tikvwal</u> gssspnft |
| 181 | le gh ekg | vncidyysggdk | pyl | isgad <u>d</u> rl <u>vkiwd</u> yqnkt |
| 221 | cvqtle gh aq | nvscasfhpe | lp | iiitgse <u>dgtvriwh</u> sst |
| | | | | |
| | | | | |

yrlestlnyg mervwcvasl rgsnnvalgy degsiivklgreepamsmda
318 ngkiiwakhs evqqanlkam gdaeikdger lplavkdmgs
351 ceiypqtiqh npngrfvvvc gdgeyiiyta malrnksfgs aqefawahds
401 seyairesns vvkifknfke kksfkpdfga esiyggfllg vrsvnglafy
451 dwentelirr ieiqpkhifw sdsgelvcia teesffilky lsekvlaaqe
501 thegvtedgi edgfevlgei qeivktglwv gdcfiytssv nrlnyyvgge
551 ivtiahldrt myllgyipkd nrlylgdkel nivsysllvs vleyqtavmr
601 rdfsmadkvl ptipkeqrtr vahflekqgf kqqaltvstd pehrfelalq
651 lgelkiayql aveaeseqkwkqlaelaisk cpfglaqecl hhaqdyggll
701 llatasgnas mvnklaegae rdgknnvafm syflqgklda clellirtgr
751 lpeaaflart ylpsqvsrvv klwrenlskv nqkaaeslad pteyenlfpg
801 lkeafvveew vkethadlwp akqyplvtpn eernvmeeak gfqpsrsaaq
851 qeldgkpasp tpvivtsqta nkeeksllel evdldnleie didttdinld
901 edildd

Fig. 14

CDC4 / CDC20 protein

```
1 mgsfplaefp lrdipvpysy rvsggiassg svtalvtaag thrnsstakt
51 vetedgeedi deyarkraag sgestpersd fkrvkhdnhk tlhpvnlant
101 gaasvdndgl hnltdisnda ekllmsvddg saapstlsvn mavashnvaa
151 pttvnaatit gsdvsnnvns atinnpmeeg alplsptass pgtttplakt
201 tktinnnnni adlieskdsi ispeylsdei fsainnnlph ayfknllfrl
251 vanmdrsels dlgtlikdnl krdlitslpf eislkifnyl afediinslg
301 vsqnwnkiir kstslwkkll isenfvspkg fnslnlklsg kypklsggdr
351 lrlsflenif ilknwynpkf
371
              vpqrttlr<u>ah</u> mtsvitclqf
                                           ednyvitgad<u>d</u>km<u>irvvd</u>si
411
              nkkfllals<u>ah</u>dgavwalkyaha
                                           gilvsgst<u>drtvrvwd</u>i
451
            kkgccthvfe ahnstvrcld iveyknikyi vtgsrdntlhvwklpkessvpdhqeehdyp
511 lvfhtpeenp yfvgvlr<u>ah</u>masvrtvsghg
                                             niv\sgsydntlivwdvaqm
561
                kclyils<u>ah</u>tddiystiydh
erkrcisasm<u>d</u>t<u>tiriwdl</u>eniwnndecsyatnsasp
618
         cak ilgamytlq<u>ah</u>ta<del>lvgllrl sdkflv</del>saaadgs<u>irgwd</u>an
```

661 dysrkfsyhh tnlsaittfy vsdnilvsgs enqfniynlr 701 sgklvhanil kdadqiwsvn fkgktlvaav ekdgqsflei ldfskaskin 751 yvsnpvnsss sslesistsl gltrttiip

Fig. 15

GBLP -CHLAMIDOMONAS HOMOLOG

| 1 mc | uetltlratlk <u>ah</u> tnw <u>v</u> t | aiatp | ldpssntllsa | sr <u>d</u> k <u>sv</u> l <u>vwel</u> erse |
|------|--------------------------------------|--------|--------------|--|
| 51 s | snygyarkalr <u>ah</u> shf <u>v</u> a | dvvi | ssdgqfcltg | sw <u>dgtlrlwdl</u> ntgtttr |
| 101 | rfv <u>ah</u> tkd <u>v</u> l | svafs | vdnrqivsg | sr <u>d</u> k <u>tiklwn</u> tlgeck |
| 141 | ytigepe gh tew <u>v</u> s | cvrfs | pmttnpiivsg | gw <u>d</u> km <u>vkvwnl</u> t |
| 183 | ncklknnlv gh hgyvn | tvtv | spdgslcasg | gk d giam <u>lwdl</u> aegkrly |
| 231 | sldagdvi <u>h</u> clcfs | pnryw | lcaatqssik | w <u>d</u> les <u>k</u> s <u>i</u> vddl |
| 273 | rpefnitskkaqvpy | cvslav | vsadgstlysgy | rt <u>dgqirvwav</u> ghsl |
| | | | | |

Fig. 16

cop-1 protein

1 meeistdpvv pavkpdprts svgeganrhe nddggsggse igapdldkdl 51 lcpicmqiik dafltacghs fcymciithl rnksdcpccs qhltnnqlyp 101 nflldkllkk tsarhvskta spldqfreal qrgcdvsike vdnlltllae 151 rkrkmeqeea ernmqilldf lhclrkqkvd elnevqtdlq yikedinave 201 rhridlyrar drysvklrml gddpstrnaw pheknqigfn snslsirggn 251 fvgnyqnkkv egkaqgsshg lpkkdalsgs dsqslnqstv smarkkriha 301 qfndlqecyl qkrrqladqp nskqendksv vrregysngl adfqsvlttf 351 trysrlrvia eirhgdifhs anivssiefd rddelfatagvsrcikvfdf

- 401 ssvvnepadmqcpivemstrsk<u>l</u>sclswnk heknhi<u>assd</u>yegi<u>vtvwdv</u> 451 ttrqslmeteenekraws<u>v</u>dfsrte psmlvs<u>as</u>d<u>d</u>c k<u>vkvw</u>ctrqeasvi
- 501 nidmkanicc vkynpgssny iavgsadhhi
- 531 hyydlrnisaplhvfs<u>ah</u>kka<u>v</u>symkflsnnelas<u>ast d</u>s t<u>lrlwdv</u>
- 551 kdn lpvrtfrght neknfvgltvnseylacgse
- 601 ttryvyhkei trpvtshrfg spdmddaekr qvptllvrfa
- 651 grvivprc

Fig. 17

CORO PROTEIN

| fgv | savwdsnyvaantry iwd aagggsfa | pfnenlvgsvse <u>d</u> cn <u>iciw</u> gip | adnvavts <mark>sgdfl<u>v</u>kt<u>md</u>ve</mark> | ck <u>d</u> kkar v£d |
|-----|---|--|---|---------------------------------------|
| | savwdsny | pfnenlvgsv | adnvavts | |
| | napkkeecyanlktk | vldiafh | kvgtisfgpv | itscehngsqivtt |
| | mskvvrsskyr <u>h</u> vfalqpkkeecyqnlktk | 61 veaiphsgkttsvplfn <u>gh</u> ksa <mark>v</mark> ldiafh | 111 eggltdsist plqtls gh kr kvgtisfgpv | agknlttve gh sdmitscehngsqivtt |
| | П | 61 | 111 | 161 |

difqgdiypd tyagepslta eqwvsgtnae pktvslaggf vkkasavefk lsefksatpq rglcflpkrc Intseceiar glkvtpftve pisfrvprks prtnsivnev vchagvknsr aifakdkvit vgfsktsere lhiydpraft tplsaqvvds asgllmpfyd adnsilylag kgdgniryye lvdespyihf pvvqvqegpk nekelreeye klkirvayle seivkkdaki keltn 3**0**1 351 251

Fig. 18

Coronin (p55)

 $1\ \mathsf{mskvvrsskyrhvf} a a q p k keecyqnlkvtk sawdsnyvaan tryfgv \underline{i\,\mathbf{wd}} a a g g g s f a v$

61 ipheasgkttsvplfn**gh**ksdvldiafhpfnenlvgsvse**d**cnic**iw**gipeggltdsist

121 plqtls**gh**krkvgtisfgpvadnvavtssg**d**flv**k**t**wd**ve

161 qgknlttve**gh**sdmitscewn hngsqivttck**d**kka**rvfd**prtnsivnev

vchqgvknsr aifakdkvit vgfsktsere lhiydpraft
tplsaqvvds asgllmpfyd adnsilylag kgdgniryye lvdespyihf
lsefksatpq rglcflpkrc lntseceiar glkvtpftve pisfrvprks
difqgdiypd tyagepslta eqwvsgtnae pktvslaggf vkkasavefk
pvvqvqegpk nekelreeye klkirvayle seivkkdaki keltn

Fig. 19

CSTF 50kDa

- myrtkvglkd rqqlykliis qllydgyisi anglineikp qsvcapseql
 lhliklgmen ddtavqyaig rsdtvapgtg idlefdadvq tmspeaseye
 tcyvtshkgp crvatysrdg qliatgsada sikildterm laksampiev
 mmnetaqqnm
- 201 enhpvirtly<u>dh</u>vdevtclafhpte qilasesr<u>d</u>ytlk<u>lfd</u>yskpsakra
- 210 fkyiqeaeml rsisfhpsgd filvgtqhpt lrlydintfqcfvsc

npqdqhtdaicsvnyns sanmyvtqskdgciklwdgvsnrcittf

npqdqhtdaicsvnyns sanmyvtqskdgciklwdgvsnrcittf

ekahdgaevcsaifsknskyilssgkdsvaklweistgrtlvrytgagls

grqvhrtqavfnhte dyvllpdertislccwdsrtaerrn

llslghnnivrcivh sptnpgfmtcsddfrarfwyrrstt d

Fig. 20

G-Beta 1 bovine

1 mseldqlrqe aeqlknqird arkacadatl sqitnnidpv griqmrtrrt

 ${\tt 85~yttnkvhaiplrsswvmtcayapsgnyvacggldnicsiynlktregnvrvsrela}$

| nqivtssg d ttca <u>lwdi</u> etg | ghtgylscc | 141 |
|---|----------------------------|-----|
| dtrlfvsgac <u>d</u> asak <u>lwdv</u> regmcrq | qqtttft gh tgdvmsl: | 174 |
| ongna fatgsd <u>d</u> atcrl <u>fd</u> lradqe | tft <u>ah</u> esdin a | 221 |
| sksgrlllagyd <u>d</u> fncn <u>vwd</u> al kadrag | lmtys <u>h</u> dni cgit | 261 |
| rtddgmavatgsw <u>d</u> sflk <u>iwn</u> | vla <u>gh</u> dnryscl | 307 |
| sksgrlllagyd <u>d</u> fncn <u>vwd</u> al kadro | lmtys <u>h</u> dniicgii | 261 |

Fig. 21

G-Beta- bovine (2)

1 rnqirdarka cgdstltqit agldpvgriq

31 mrtrrtlr<u>ah</u>lakiyamhwgtdsr llvsasq<u>dg</u>kli<u>iwd</u>s

71 egnvryttnkvhaiplrsswvmtcayapsgnfvacggldnicsiyslktr

vsrelpghtgylsccrfldd nqiitssgdttcalwdietg

qqtvgfaghsgdvmslslap dgrtfvsgacdasiklwdvr

dsmcrqtfighesdinavaffp ngyafttgsddatcrlfdlradq

ellmyshdniicgitsvafsrsgrlllagyddfncniwdamkgdr

agvlaghdrrvsclgvt ddgmavatgswdsflkiwn

Fig. 22

G- BETA DROSOPH

1 mneldslrqe aeslknaird arkaacdtsllqaatslepigriqmrtrrt

1rghlakiyamhwgn dsrnlysasqdgkli<u>vwd</u>shttnkv

91 haiplrsswvmtcayapsgsyvacggldnmcsiynlktregnvr

vsrelpghggylsccrfl ddnqivtssgdmscglwdietglqv
tsflghtgdvmalsla pqcktfvsgacdasaklwdiregvckq
tfpghesdinavtf fpngqafdtgsddatcrlfdiradqe
lamyshdniicgitsvafsksgrlllagyddfncnvwdtm
and kaersgilaghdnrvsclg vtengmavdtgswdsflrvwn

Fig. 23

G-BETA HUMAN

| 1 mt | eqmtlrgtlk gh ng | wvtqiattp | qfpdmil | sasr <u>d</u> k <u>ti</u> i <u>mwkl</u> trdet |
|------|-------------------------|--------------|----------|---|
| 51 r | nygipqralr <u>gh</u> sh | fvsdvvi | ssdgqfal | sgsw <u>dgtlrlwdl</u> ttgtttrr |
| 101 | fv <u>ah</u> tk | dvlsvaf | ssdnrqiv | sgsr d k <u>tiklwn</u> tlgvcky |
| 141 | tvqde <u>sh</u> se | wvscvrfsp | nssnpiiv | scgw <u>d</u> klv <u>kvwnl</u> a nc |
| 183 | klktnhi gh tg | ylntvtv | spdgslca | sggk <u>dg</u> qam <u>lwdl</u> |
| 222 | negk <u>h</u> ly | tldggdiinald | fspnrywl | caatgpsi <u>kiwdl</u> egkiivdel |
| 271 | kqevistsskaepp | actslawsad | gqtlf | agyt <u>d</u> nlv <u>rvwqv</u> tigtr |
| | | | | |

Fig. 24

G-Beta 2 (Human)

1 mseleqlrqe aeqlrnqird arkacgdstl tqitagldpv griqmrtrrt

51 lr<u>gh</u>lakiya mhwgtds rllvsasq<u>dg</u>kli<u>iwd</u>syt

97 tnkvhaiplrsswvmtcayapsgnfvacggldnicsiyslktre

| 151 | gnvrvsrelp <u>ah</u> to | ylsccrfl | ddnqiitss | g <u>d</u> ttca <u>lwdi</u> etgqqtvgf |
|-----|-------------------------|---------------|-----------|---------------------------------------|
| 201 | a gh s | dvmslslap | dgrtfvsgd | c <u>d</u> asik <u>lwdv</u> rdsmcrq |
| 241 | tfi gh es | dinavaffpn | gyafttgs | d <u>d</u> atcr <u>lfd</u> lradqe |
| 281 | llmy <u>sh</u> di | niicgitsvafsr | sgrlllagy | d <u>d</u> fncn <u>iwd</u> am |
| 321 | kgdragvla gh dı | rvsclgvtddgm | ı avatgs | w d sflk <u>iwn</u> |

Fig. 25

. //. // ////

25/53

G-Beta 4 (mouse)

- 1 seleqlrqeaeqlrnqiqdarkacndatlvqitsnmdsv griqmrtrrt
- 51 lr**ah**lakiyamhwgydsr llvsasq**d**gkli**iwd**syttnkm
- 91 haiplrsswvmtcayapsgnyvacggldnicsiynlktregdvrvsrela
- 141 **gh**tgylsccrflddg qiitssg**d**ttca**lwdi**etgqqtttf

 181 t**gh**sgdvmslslspd lktfvsgac**d**assk**lwdi**rdgmcrq

 221 sft**gh**isdinavsffpsg yafatgsd**d**atcrl**fd**lradqe

 261 llly**sh**dniicgitsvafsksgrlllagyd**d**fncs**vwd**alkggrs

 306 gvla**gh**dnrvsclgv tddgmavatgsw**d**sflr**iwn**

Fig. 26

GROUCHO PROTEIN DROSOPH

1 mypspvrhpa aggpppqgpi kftiadtler ikeefnflqa hyhsiklece 51 klsnektemq rhyvmyyems yglnvemhkq teiakrlntl inqllpflqa 101 dhqqqvlqav erakqvtmqe lnliigqqih aqqvpggppq pmgalnpfga 151 lgatmglphg pqgllnkppe hhrpdikptg legpaaaeer lrnsvspadr 201 ekyrtrspld iendskrrkd eklqedegek sdqdlvvdva nemeshsprp 251 ngehvsmevr dreslngerl ekpsssgikq erppsrsgss ssrstpslkt 301 kdmekpgtpg akartptpna aapapgvnpk qmmpqgpppa gypgapyqrp 351 adpyqrppsd paygrpppmp ydphahvrtn giphpsaltg gkpaysfhmn 401 gegslqpvpf ppdalvgvgi prharqintl shgevvcavt isnptkyvyt 451 ggkgcvkvwdisqpgnknpv sqldclqrdn yirsvkllpdgrtlivggea 501 snlsiwdlas

ptpri kael<u>ts</u>aapacyal aspd<u>skv</u>cfsccs<u>dgniavwdl</u>

hneilvrqfq<u>gh</u>tdgascidispdg<u>srl</u>wt ggl<u>d</u>nt<u>v</u>rs<u>wdl</u>regrql

601 qqhdfssqif slgycptgdwlavgmenshv evlhaskpdk yqlhlhescv 651 lslrfaacgkwfvstgkdnl lnawrtpyga sifqsketss vlscdistdd 701 kyivtgsgdk katvyeviy

1 mtselealrqeteqlknqirearkaaadttlamatanvepvgriqmrtrr

GTP binding protein (squid)

51 tlr<u>ah</u>lakiyamhwasd srnlvsasq<u>dg</u>kliv<u>wdg</u>yttnk

91 vhaiplrssw vmtcayapsg nyvacggldn icsiyslktr egnvrvsrel

dnqivt\$sgdmtcalwnietgnqits gvtedgm<u>a</u>vatgs<u>wd</u>sflkiw n mrtfvs∮ac<u>d</u>asakl<u>fd</u>irdgick gfafat**ý**sd<u>d</u>atcrl<u>fd</u>iradq 261 eigmy<u>sh</u>dniikgitsvafsksgrlllggyd<u>d</u>fncnv<u>wd</u>v 221 qtft**gh**esdi<mark>h</mark>aityfpn 181 fg<u>ah</u>tgdvmslslapd 141 pghtgylsccrfid 301 lkqeragvlaghdnryscl

IEF SSP 9306

1 madkeaafdd aveervinee ykiwkkntpf lydlvmthal ewpsltaqwl 51 pdvtrpegkd fsihrlvlgt htsdeqnhlv iasvqlpndd aqfdashyds 101 ekgefggfgs vsgkieieik inhegevnra rympqnpcii atktpssdvl 151 vfdytkhpsk pdpsgecnpd

171 lrlrghakeg yglswnpnlsg hllsasddhticlwdisav
pkegkvvdak

221 tiftghtavv edvswhllhe slfgsvaddaklmiwdtrsn
261ntskpshsvdahtaevnclsfnpysefilatgsadktvalwdlrnl
307 klklhsfeshkdeifavawsphnetilassgtdrrlnvwdls
351 kigeeaspedaedgppellfihgghtakisdf swnpne

387 pwvicsvsednimqvwqmelvldh

HUMAN 12.3

| 1 | mteqmtlrgtlk gh ng | ywvtqiattpqfpdm | ilsasr <u>d</u> k <u>ti</u> i <u>mwkl</u> trdet |
|----|---------------------------|---------------------|---|
| 51 | nygipqralr <u>ahs</u> l | nfvsdvvissdgq | falsgsw <u>dgtlrlwdl</u> tt |
| 95 | gtttrrfv ght | dvlsvafssdn | rqivsgsr <u>d</u> k <u>tiklwn</u> tlg |
| 13 | 7 vcky tvqde <u>shs</u> | ewvscvrf spn | ssnpiivscgw <u>d</u> kl <u>vkvwnl</u> a |
| 18 | 1 ncklktnhi ght | ylntvtvs | pdgslcdsggk <u>d</u> gqam <u>lwdl</u> n |
| 22 | egk <u>h</u> ly | tldggdii nalc | fspnrywlcaatgp <u>sikiwdl</u> e |
| 26 | 3 gkiivdelkqevist | sskaeppqctslaws | sadgqtlfagyt <u>d</u> nl <u>vrvwqv</u> tigtr |

Fig. 30

IEF -7442 - human

1 maskemfedt veervineey kiwkkntpfl ydlvmthalq wpsltvqwlp
51 evtkpegkdy alhwlvlgth tsdeqnhlvv arvhipndda qfdashcdsd
101 kgefggfgsv tgkieceiki nhegevnrar ympqnphiia tktpssdvlv
151 fdytkhpakp dpsgecnpdl

171 rlrghqkegyglswnsnlsghllsasddhtvclwdinagpkegkivdaka
221iftghsavvedvawhllheslfgsvaddqklmiwdtrsnt
261 tskpshlvdahtaevnclsfnpysefilatgsadktvalwdlrnlklklh
311 tfeshkdeifqvhwsphneti lassgtdrrlnvwdlskigeeqsaedaed
361 gppellfihgghtakisdfswnpnepwvicsvsednimqiwamaeniynd

411 eesdvttsel egggs

insulin-like growth factor binding protein complex

1 malrkgglal allllswval gprslegadp gtpgeaegpa cpaacvcsyd

51 ddadelsvfc ssrnltrlpd gvpggtqalw ldgnnlssvp paafqnlssl

101 gflnlqggql gslepqallg lenlchlhle rnqlrslalg

141 tfahtpalaslglsnnrlsrledglfeglgslwdlnlgwn slavlpdaaf rglgslrelv

201 lagnrlaylq palfsglael reldlsrnal raikanvfvq lprlqklyld
251 rnliaavapg aflglkalrw ldlshnrvag lledtfpgll glrvlrlshn
301 aiaslrprtf kdlhfleelq lghnrirqla ersfeglgql evltldhnql
351 qevkagaflg ltnvavmnls gnclrnlpeq vfrglgklhs lhlegsclgr
401 irphtftgls glrrlflkdn glvgieeqsl wglaelleld ltsnqlthlp
451 hrlfqglgkl eylllsrnrl aelpadalgp lqrafwldvs hnrlealpns

501 llaplgrlry lslrnnslrt ftpqppgler lwlegnpwdc gcplkalrdf 551 alqnpsavpr fvqaicegdd cqppaytynn itcasppevv gldlrdlsea 601 hfapc

Fig. 32

SUBSTITUTE SHEET (RULE 26)

insulin like growth factor binding protein complex - rat

1 malrtggpal vvllafwval gpchlqgtdp gasadaegpq cpvactcshd
51 dytdelsvfc ssknlthlpd dipvstralw ldgnnlssip saafqnlssl
101 dflnlqgswl rslepqallg lqnlyylhle rnrlrnlavg

141 lfthtpslaslslssnllgrleeglfaglshlwdlnlgwn

181 slvvlpdtvf qglgnlhelv

201 lagnkltylq palfcglgel reldlsrnal rsvkanvfvh lprlqklyld

251 rnlitavapg aflgmkalrw ldlshnrvag lmedtfpgll glhvlrlahn

301 aiaslrprtf kdlhfleelq lghnrirqlg ertfeglgql evltlndnqi

351 tevrvgafsg lfnvavmnls gnclrslper vfqgldklhs lhlehsclgh

401 vrlhtfagls glrrlflrdn sissieeqsl aglselleld lttnrlthlp

451 rqlfqglghl eylllsynql ttlsaevlgp lqrafwldis

491 hnhletlaeglfsslgrvrylslrnnslqtfspqpglerlwldanpwdcs

541 cplkalrdfa lqnpgvvprf vqtvcegddc qpvytynnit cagpanvsgl dlrdvsethf

601 vhc

LIS1 (human)

- 1 mvlsqrqrde lnraiadylr sngyeeaysv fkkeaeldvn eeldkkyagl
- 51 lekkwtsvir lqkkvmeles klneakeeft sggplgqkrd pkewiprppe
- 101 kyals<u>ah</u>rspytrvifhpyfsymysase<u>d</u>atik<u>ywd</u>yetg
- 151 dfertlk<u>ah</u>tds/qdisfdhsgkllasc\$a<u>d</u>mtik<u>lwd</u>fqgfecir
- 191 tmh<u>ah</u>dhnyssvaimpngdhivsa\$r<u>d</u>ktikm<u>wev</u>qtgycvktf
- 241 t<u>ah</u>rew/rmvrpnqdgtliasc\$n<u>d</u>qtvr<u>vw</u>vvatkecka
- 291 elrehehvveciswapessy
- 311 ssiseat<u>as</u>etkksgkpgp fllsg\$r<u>d</u>kt km<u>wdv</u>stgmc
- 351 lmtlvghdnwvrgvlfhsggkfilscddktlr<u>vwd</u>yknk
- 391 rcmktlna<u>h</u>ehfytsldfhktapyvvtg\$v<u>d</u>qtvk<u>vwe</u>cr

Fig. 34

MD6

1 merkdfetwl dnisvtflsl mdlqknetld hlislsgavq lrhlsnnlet 51 llkrdflkll plelsfyllk wldpqtlltc clvskqrnkv isactevwqt 101 acknlgwqid dsvqdslhwk kvylkailrm kqledheafe

| | | | | _ |
|-----|--------------------|---------------------|--------|--|
| 141 | tssli gh so | rvyalyyk | dgllct | gsd <u>d</u> l <u>s</u> a <u>klwdv</u> stgqc |
| 181 | vygiqt <u>h</u> to | a avkfde | qklvt | gsf <u>d</u> n <u>tv</u> ac <u>wew</u> ssgart |
| 220 | qhfr gh tg | avfsvdysdel | dilvs | gsa <u>d</u> fa <u>vkvw</u> a <u>l</u> sagtc |
| 261 | lntlt gh te | wvtkvvlqkckvksllhsp | gdyill | sa <u>d</u> k y ei <u>kiw</u> p <u>i</u> grei |
| | | | | |

301 nckclktlsv sedrsiclap rlhfdgkyiv cssalglyaw 351dfasydilrv iktpevanla llgfgdvfal lfdnhylyim dlrteslisr 401wplpeyrksk rgtsflager pg

Fig. 35

MSL1

1 mnqcakdith eassipidlq eryshwkknt kllydylntn stkwpsltcq
51 ffpdldttsd ehrillssft ssqkpedeti yiskistlgh ikwsslnnfd
101 mdemefkpen strfpskhlv ndisiffpng ecnrarylpq npdiiagass
151 dgaiyifdrt khgstrirqs kishpfetkl fgshgviqdv eamdtssadi
201 neatslawnl qqealllssh sngqvqvwdi kqyshenpii dlplvsinsd
251 gtavndvtwm pthdslfaac tegnavslld lrtkkeklqs

291 nrek<u>h</u>dggvnscrfn yknslilasa<u>d</u>sngrlnl<u>wd</u>irnmn
331 kspiatme<u>h</u>gtsvstlewspnfdtvlatagqe<u>d</u>gl vkl<u>wd</u>tsceetifth
381 g<u>gh</u>mlgvndisw dahdpwlmcsvan<u>d</u>n svhi<u>w</u>kpagnlvg hs

MUS MUSCULUS PROTEIN

sledsdnfis clensyipqn vengevveeq slgrrfhpye leagevvegq gggslfypye leagevveaq nvqnlfhrye leegevveaq vvqsmfpyye leagevveae evagffarye learevigaa ggaglsrhyg leggevveat 251 avrrliqhhe leegedvddq eessemheet sedsseqydi eddslidewi 51 ssdvtgteds svltpqstdv nsvdsyqgye gddddeedde ddkdgdsnlp 1 msshesytna aetpenisil sclgetsgal vdtktisdik tmdprvsltp aletsplprp rwnvlsalrd rqlgssgrfv yeacgarlfv qrfs 201 301 151 101

fnqhgt lasgsd**dlkvivwdw**lkkrsvln

351 lehvfeghsgqvntvh

Fig. 37A

.

fdsghknnilgakflpncnd ailamcgrdg qvrvaglsav

401 agthmtkrlv khggashrlglepdspfrfl tsgedavvfn

451 idlrqahpas kllvikdgdk kvglytvfvn

panvyqfavg gqdqfmriyd qrkidenvnn gvlkkfcphh llssdypahi 501

tslmysydgt eilasynded iyifnssdsd gaqyakrykg hrnnstvkgv 551

601 yfygprsefv

611 msgsdc $oldsymbol{gh}$ ifi $oldsymbol{h}$ eksscqiv qfleadeggt incidshpylpvl $oldsymbol{h}$ esgl $oldsymbol{dhev}$ ki $oldsymbol{w}$ spiae

671 pskklaglkn vikinklkrd nftlrhtslf 701nnsmlcflms hvtqsnygrswrgirinagg gdfsdsssss eetnqes

Fig. 37B

ORF RB1

1 mnqcakdith eassipidlqeryshwkknt kllydylntn stkwpsltcq 51 ffpdldttsd ehrillssft ssqkpedeti yiskistlghikwsslnnfd 101 mdemefkpen strfpskhlv ndisiffpng ecnrarylpq npdiiagass 151 dgaiyifdrt khgstrirqs kishpfetkl fgshgviqdv eamdtssadi 201 neatslawnl qqealllssh sngqvqvwdi kqyshenpii dlplvsinsd 251 gtavndvtwm pthdslfaac tegnavslld lrtkkeklqs

nrekhdggvnscrfnykn slildsadsngrlnlwdirnmn

331 kspiatmehgtsvstlewspnfdtvlatagqedg l<u>vklwd</u>tsceetifth

381 gghmlgvndiswdah dpwlmcsvandn s<u>vhiwk</u>pagnlvghs

Periodic Trp protein

1 misatnwvpr gfssefpeky vlddeeveri nqlaqlnldd akatleeaeg
51 esgveddaat gssnklkdql didddlkeyn leeyddeeia dneggkdvsm
101 fpglsndsdv kfhegekged pyislpnqed sqeekqelqv ypsdnlvlaa
151 rteddvsyld iyvyddgagf hssdipveeg deadpdvarg lvrdpalyvh
201 hdlmlpafpl cvewldykvg snseeaanya aigtfdpqie iwnldcvdka
251 fpdmilgepl dnsmvslksk

271 kkkkkskt<u>ah</u> itthhtdavl smahnkyfrsvlastsa<u>d</u>htv kl<u>wd</u>lnsgn 321 aarslasi<u>h</u>s nknvsssewhmlngsilltggydsrvaltavris<u>d</u>esqmsky<u>w</u>samagee

- -- 381 ietvtfasen iilcgtdsgn vysfdirnne nrkpvwtlka
- 421 hdagistlcs nkfipgmmst gamgektvkl
 - 451 wkfplddatn tkgpsmvlsr dfdvgnvlts sfapdievag tmviggvnkv
 - 501 lklwdvftnr svrksfksel envqarakee aqkigkssri arkytsndnp 551 dtvitiddqg edeeereggd ehddma

PLAP

1 mhymsghsnf vsyvciipss diyphgliat ggndhnicif sldspmplyi

- 51 lkahkdtvcslssgkf gtllsgswdttakvwlndkcmmtl
- 91 q<u>ah</u>tфavwavkilpeqglm|tgsa<u>d</u>k<u>tiklwk</u>agrcertf
- 131 lahedcvrglails eteflscandasirrwaitgeclevy
- 171 f<u>gh</u>thyiysisvfpnskdf**y**ttae<u>d</u>r<u>slriwk</u>hgecaqti
- 211 rlpaqsiwcc cvlengdivv gasdgiirvf teseertasa
- 251 eeikaslsre spliakvltt eppiitpvrr tlpcrvtrsm issclsrlvs
- 301 tslstsdshl titalhlflt tttte

RETINOBLASTOMA BINDING PROTEIN - HUMAN

1 madkeaafdd aveervinee ykiwkkntpf lydlvmthal ewpsltaqwl

51 pdvtrpegkd fsihrlvlgt htsdeqnhlv iasvqlpndd aqfdashyds

101 ekgefggfgs vsgkieieik inhegevnra rympqnpcii atktpssdvl

151 vfdytkhpsk pdpsgecnpd

lsghl∥sasd**d**hticl**md**isavpkegkvvdak heslfgsvaddaklmi<u>wd</u>trsn lrlrghqkegyglswnpn tiftghtavvedvswhll 171 221

261 ntskp<u>sh</u>svdahtaevnclsfnpysefildtgsa**d**ktval**wd**lrnlklkl

netildssgt**d**rrlnv**md**lskigeeqspedaedgppell hsfe<u>sh</u>kdei|fqvqwsph 311

fihg<u>ah</u>taki|sdfswnpnepw

374

vidsvse<u>d</u>nimqv**mg**maeniyndedpegsvdpegqgs

•

42/53

S253 PROTEIN

1 mfksktstls ydetpnsneg drnatpvnpk eksqtkhlni pgdrsrhssi 51 adskrsssry dggysadiip aqlrfidnid ygtrlrktlh rnsvvsngyn 101 klsendrwyf dlfdrkyfen yleeptyiki fkkkegleqf drmflaqelk 151 ipdvykstty qgepavanse lfknsiccct fshdgkymvi gckdgslhlw 201 kvinspvkrs emgrseksvs asranslkiq rhlasisshn gsissndlkp 251 sdqfegpskq lhlyapvfys

271 dvfrvfmehaldildanw skngflitasmdktaklwhper
311 kyslktfvhpafvtsaiffpnddrfiitgcldhrcrlwsi

351 ldnevsyafd ckdlitsltl sppggeytii gtfngyiyvl lthglkfvss
401 fhvsdkstqg ttknsfhpss eygkvqhgpr itglqcffsk vdknlrlivt
451 tndskiqifd lnekkplelf kgfqsgssrh rgaflmmkne pvvftgsddh
501 wfytwkmqsf nlsaemncta phrkkrlsgs mslkgllriv snkstndecl
551 tetsnqsssh tftnssknvl qtqtvgsqai knnhyisfha hnspvtcasi
601 apdvaiknls lsndlifelt sqyfkemgqn ysesketcdn kpnhpvtetg
651 gfssnlsnvv nnvgtilitt dsqglirvfr tdilpeirkk iiekfheynl
701 fhleaagkin nhnndsilen rmderssted nefsttppsn thnsrpshdf
751 celhpnnspv isgmpsrasa ifknsifnks ngsfislksr sestsstvfg
801 phdiprvstt ypklkcdvcn gsnfecaskn piaggdsgft cadcgtilnn
851 fr

S0F1

mkiktikrsa ddyvpvkstq esqmprnlnp elhpferare ytkalnatkl

aiaknygslnklatdsa<u>dg</u>viky<u>wn</u>mstr ermfakpfvgqlgy**gh**rddvy 51

eefvsfkahyglvtg<u>l</u>cv†qprfhdkkpdlksqnfmlsdsd<u>d</u>ktvk<u>l**ws**invddysnkns</u> 101

sdndsvtneeglir#fdgesafqgidshrenstfdtggakihl<u>wd</u>vnrlk

161

pvsdlswgad nitslkfnqn etdilastgs dnsivlydlr tnsptqkivq tmrtnaicwn 211

pmeafnfvta nedhnayyyd mrnlsrslnv fkdhvsavmd vdfsptgdei vtgsydksir 271

iyktnhghsreijyhtkrmqhvf vkysmdskyiisgsddgnvrlmcskaw 331

ersnvkttre knkleydekl kerfrhmpei krisrhrhvp qvikkaqeik 381

nielssikrr eanerrtrkdmpyiserkką ivgtvhkyed sgrdrkrrke ddkrdtqek 431

STE4 - YEAST

| 1 | maahqmdsit ysnnvtqqyi qpqslqdisa vedeiqnkie aarqeskqlh |
|-----|---|
| 51 | aqinkakhki qdaslfqman kvtsltknki nlkpnivl |
| 89 | k gh nnkisdfrwsrdsk rilsdsq d gfml <u>iwd</u> sasglkqnai |
| 131 | pldsqwvlscaispsstlvasaglnnnctiyrvskenrva |
| 171 | qnvasifk gh tcyisdieft dnahiltasg <u>d</u> mtca <u>lwdi</u> p |
| 211 | kakrvreysd <u>h</u> lgdvlalaipeepnlenssntfascgs <u>dg</u> yty <u>iwd</u> srsp |
| 261 | savqsfyvndsdinalrffkdgmsivagsd ngainmydlr |
| 301 | sdcsiatfslfrgyeertptptymaanmey ntaqspqtlk |
| | |
| 341 | stsssy <u>ld</u> napvvsldfsasgrlmyscyt <u>d</u> igcv <u>vwd</u> vlk |
| 381 | geivgkle gh ggrvtgvrsspdglavctgsw d stmk <u>iws</u> p gyq |

Fig. 44

F

TRANSCRIPTION FACTOR TIIF

elakfiddds fdaqhyeqay kelrtfveds ldiykhelsm vlypilvqiy fkilasglre kakefiekyk cdldgyyieg lfnllllskp eellendlvv ameqdkfvir msrdshslfk rhiqdrrqev vadivskylh fdtyegmarn klqcvatags hlgeakrqdn kmrvyygllk evdfqtlttp apapeeeddd pdapdrpkkk kpkkdpllsk ksksdpnaps idriplpelk dsdkllklka 51 velseisesd vqqvlgavlg agdanrerkh vqspaqghkq savteanaae 1 mslevsning gngtqlshdk rellcllkli kkyqlkstee llcqeanvss lreaskrlal skdqlpsavfytvln 151 101 201 251 301

Fig. 45A

\$

shqgvtcaeisddstm lacgfgdssv**riw**sltpanvrtlkdads

376

lreldkesadi

431 nvrmlddrsgevtrslmghtdpvyrcafapemnll¶scsedstirlWsll

twscvvtyrghvypvwdvrfaphgyyfyscsy<u>d</u>k<u>tarlw</u>atdsnqalrvf

481

531

vghlsdvdcvqfhpnsnyvdtgss<u>drtvrlmd</u>nmtgqsvr

lmtghkgsvsslafsacgryldsgsv<u>d</u>hnii**imdl**sngsl

vttllrhtstvttitfsrdgtvldaagldnn1t1md£hkv

651 tedyisnhit vshhqdende dvylmrtfps knspfvslhf trrnllmcvg 701 lfks

Fig. 45B

SUBSTITUTE SHEET (RULE 26)

571

611

TUP1

1 mtasvsntqn klnelldair qeflqvsqea ntyrlqnqkd ydfkmnqqla 51 emqqirntvy elelthrkmk dayeaeikhl klgleqrdhq iasltvqqqq 101 qqqqqqqqq hlqqqqqla aasasvpvaq qppattsata tpaantttgs 151 psafpvqasr pnlvgsqlpt ttlpvvssna qqqlpqqqlq qqqlqqqpp 201 pqvsvaplsn taingsptsk etttlpsvka pestlketep ennntskind 251 tgsattattt tateteikpk eedatraslh qdhylvpynq ranhskpipp 301 flldldsqsv pdalkkqtnd yyilynpalp reidvelhks ldhtsvvccv 351 kfsndgeyla tgcnkttqvy rvsdgslvar lsddsaannh rnsitenntt 401 tstdnntmtt tttttitta mtsaaelakd venlntsssp

| | j | | |
|-----|-----------------------|----------------|--|
| 441 | ssdly | irsvcfspdgkfla | tgae <u>d</u> rli <u>riwdi</u> enrkivmi |
| 481 | lq ah eqd | iysldyfpsgdklv | sgsg d r <u>tvriwdl</u> rtgqcs |
| 521 | ltlsiedgv | ttvavspgdgkyia | agsl <u>d</u> ra <u>vrvwd</u> setgflverldsene |
| 571 | sgt gh kds | vysvvftrdgqsvv | sgsl <u>d</u> r <u>svklw</u> nlqnannksdsktpnsg |
| 621 | tcevtyi gh kdf | vlsvattqndeyil | sgsk <u>d</u> rg <u>v</u> l <u>fwd</u> kk |
| | | | |

661 sgnpllmlqg hrnsvisvav angsslgpey nvfatgsgdc 701 kariwkykki apn

TUP1 HOMOLOG

| 1 | msqkqstnqn | qngthqpqpv | knqrtnnaag | ansgqqpqqq | sqgqsqqqgr |
|-----|------------|------------|------------|------------|------------|
| 51 | sngpfsasdl | nrivleylnk | kgyhrteaml | raesgrtltp | qnkqspantk |
| 101 | tgkfpeqssi | ppnpgktakp | isnptnlssk | rdaeggivss | grleglnape |
| 151 | nyiraysmlk | nwwdssleiy | kpelsyimyp | ifiylflnlv | aknpvyarrf |
| 201 | fdrfspdfkd | fhgseinrlf | svnsidhike | nevasafqsh | kyritmsktt |
| 251 | Inlllyflne | nesiggslii | svinahldpn | ivesvtarek | ladgikvlsd |
| 301 | sengngkqnl | emnsvpvklg | pfpkdeefvk | eietelkikd | dqekqlnqqt |
| 351 | agdnysgann | rtllqeykam | nnekfkdntg | dddkdkikdk | iakdeekkes |
| 401 | elkvdgekkd | snlsspardi | lplppktald | lkleiqkvke | srdaikldnl |
| 451 | qlalpsvcmy | | | | |

| 461 | tfqntnkdmscldfsd | dcriaaag | | fq d sy | i <u>kiw</u> s <u>l</u> dgsslnnpnialnnn |
|-----|---------------------------|----------|----------|---------------------------|---|
| 511 | dkdedptcktlv gh sg | tvystsf | spdnkyl | lsgse <u>d</u> k <u>t</u> | <u>vrlw</u> smdthtal |
| 561 | vsyk <u>gh</u> nh | pvwdvs 1 | fsplghyf | atash <u>d</u> qt | a <u>rlw</u> scdhiy |
| 601 | plrifa <u>gh</u> lr | dvdcvs 1 | fhpngcyv | ftgss <u>d</u> k <u>t</u> | c <u>rmwdv</u> st |
| 641 | gdsvrlfl gh td | pvisi av | vcpdgrwl | stgse d gi | <u>invwdi</u> gtgkr |
| 686 | lkqmr gh gk | naiyslsy | yskegnvl | isgga <u>d</u> h <u>t</u> | <u>vrvwd</u> lkkattep |

731 saepdepfig ylgdvtasin qdikeygrrr tviptsdlva 771 sfytkktpvf kvkfsrsnla laggafrp

Fig. 47



YCU7

1 mvrrfrgkel aattfnghrd yvmgaffshd qekiytvskd gavfvweftk 51 rpsddddnes edddkqeevd iskyswritk khffyanqak vkcvtfhpat 101 rllavgftsg efrlydlpdf tliqqlsmgq npvntvsvnq tgewlafgss 151 klgqllvyew

161 qsesyilkqqghfdstnslay spdgsrvvtasedgkikvwd

202 itsgfclatfeehtssvta vqfakrgqvmfsssldgtvrawdli

251 ryrnfrtftgteriqfnclavdpsgevvcagsldnfdih vwsvqt

291 gqlldalsghegpvscl sfsqensvlasaswdktiriwsi

341 fgrsqqvepi evysdvlals mrpdgkevav stlkgqisif niedakqvgn 391 idcrkdiisg rfnqdrftakilndpnfllq yitvlmvwll wlvviitpfv 431 ymmfqmksc

YCW2 PROTEIN

1 mstlipppsk kakkeaalpr evaiipkdlp nvsikfaald tgdnvggalr 51 vpgaisekal eellnalngt sddpvpytfs ctiagkkasd pvktiditdn 101 lysslikpgy nstedaitll ytpravfkvk

| 131 | pvtrsssaia gh gst | ilcsafaph | tssrmv | tgag <u>d</u> ntari <u>w</u> dcdtqtpmh |
|-----|--------------------------|---------------|----------|--|
| 181 | tlk gh ynw | vlcvswsp | dgevia | tgsm <u>d</u> ntirl <u>w</u> dpksgqc |
| 221 | lgdalr gh skw | itslswepihlvk | pgskprla | sssk <u>dg</u> tiki <u>w</u> dtvsrvc |
| 271 | qytms gh tns | vscvkwggqg | lly | sgsh <u>d</u> rtvrv <u>w</u> dinsqg |
| | | | | |

311 rcinilksha hwvnhlslst dyalrigafd htgkkpstpe

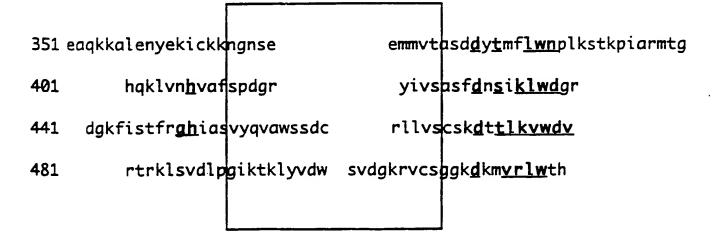


Fig. 49

Alegan .

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Fig. 50

YKL525

1 mfksktstls ydetpnsneg drnatpvnpk eksqtkhlni pgdrsrhssi 51 adskrsssry dggysadiip aqlrfidnid ygtrlrktlh rnsvvsngyn 101 klsendrwyf dlfdrkyfen yleeptyiki fkkkegleqf drmflaqelk 151 ipdvykstty

- 161 qgepavanselfknsiccct fshdgkymvi gckdgslhlwk
- 202 vinspvkrs emgrseksvs asranslkiq rhlasisshn gsissndlkp
- 251 sdqfegpskqlhlyapvfysdvf rvfmehaldildanwskngflitasmd
- 301 ktaklwhperkyslktfvhpdfvtsaiffpnddrfiitgcldhrcrlwsi

351 ldnevsyafd ckdlitsltl sppggeytii gtfngyiyvl lthglkfvss
401 fhvsdkstqg ttknsfhpss eygkvqhgpr itglqcffsk vdknlrlivt
451 tndskiqifd lnekkplelf kgfqsgssrh rgqflmmkne pvvftgsddh
501 wfytwkmqsf nlsaemncta phrkkrlsgs mslkgllriv snkstndecl
551 tetsnqsssh tftnssknvl qtqtvgsqai knnhyisfha hnspvtcasi
601 apdvaiknls lsndlifelt sqyfkemgqn ysesketcdn kpnhpvtetg
651 gfssnlsnvv nnvgtilitt dsqglirvfr tdilpeirkk iiekfheynl
701 fhleaagkin nhnndsilen rmderssted nefsttppsn thnsrpshdf
751 celhpnnspv isgmpsrasa ifknsifnks ngsfislksr sestsstvfg
801 phdiprvstt ypklkcdvcn gsnfecaskn piaggdsgft cadcgtilnn
851 fr

1

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yrb 1410 yeast

1 msqkqstnqn qngthqpqpv knqrtnnaag ansgqqpqqq sqgqsqqqgr
51 sngpfsasdl nrivleylnk kgyhrteaml raesgrtltp qnkqspantk
101 tgkfpeqssi ppnpgktakp isnptnlssk rdaeggivss grleglnape
151 nyiraysmlk nwvdssleiy kpelsyimyp ifiylflnlv aknpvyarrf
201 fdrfspdfkd fhgseinrlf svnsidhike nevasafqsh kyritmsktt
251 lnlllyflne nesiggslii svinqhldpn ivesvtarek ladgikvlsd
301 sengngkqnl emnsvpvklg pfpkdeefvk eietelkikd dqekqlnqqt
351 agdnysgann rtllqeykam nnekfkdntg dddkdkikdk iakdeekkes
401 elkvdgekkd snlsspardi lplppktald lkleiqkvke srdaikldnl
451 qlalpsvcmy tfqntnkdms cldfsddcri aaagfqdsyi kiwsldgssl
501 nnpnialnnn dkdedptckt lvghsgtvys tsfspdnkyl lsgsedktvr

Fig. 51A



551 lwsmdthtalvsykghnhpvwdvs fsplghyfatashdatarlwscdhiy
601 plrifaghlndvdcvs fhpngcyvftgssdktcrmwdvst
641 gdsvrlflghtapvisiav cpdgrwlstgsedgiinvwdigtgkrlkamr
691 ghgknaiyslsyskegnvlisggadhtvrvwdlkkattep
731 saepdepfig ylgdvtasinadikeygrrr tviptsdlva sfytkktpvf
kvkfsrsnla laggafrp

Fig. 51B